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JOURNAL OF GENERAL CHEMISTRY OF THE USSR

Volume 28, Number 6 June 1958

CONTENTS

	PAGE	RUSS. PAGE
Diene Hydrocarbons from Unsaturated Alcohols. II. Catalytic Dehydration of Tiglyl Alcohol and 2-Ethylhexen-2-ol-1 to Diene Hydrocarbons. Iu. A. Gorin, V. S. Ivanov and E. K. Khrennikova	1475	1421
Investigation of Conjugated Systems. LXXXVII. Addition of α-Chloro- and α-Bromo-Ether to Chloroprene. B. A. Vovsi and A. A. Petrov	1481	1426
Conjugated Systems. LXXXVIII. Condensation of 3-Chloro-1,3-pentadiene and 3-Chloro-1,3-hexadiene with Propargylaldehyde and Propiolic Acid. E. A. Leporskaia and A. A. Petrov	1486	1432
Conjugated Systems. LXXXIX. Influence of Various Factors on the Yield of Geranyl Chloride in the Reaction of Isoprene with Its Hydrochlorides. A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, E. Iu. Shvarts, and L. L. Cherenkova	1490	1435
Acetylene Derivatives. 193. Total Synthesis of Isoprenoid Alcohols (Linalool, Geraniol Nerol, Nerolidol, Farnesol, Geranyllinalool, Geranyl-Geraniol and Phytol). I. N. Nazarov, B. P. Gusev and V. I. Gunar	1498	1444
Simpler Analogs for Corticosteroids. I. Stereochemistry of Cyanohydrin and Acetylenic Synthesis. Configuration of 1-Cyano- and 1-Ethynyl-2-methylcyclo-hexanols. I. N. Nazarov, A. V. Kamernitskii and A. A. Akhrem	1511	1458
Investigations in the Field of Polymethylene Rings. XXX. Reaction of Diacetyl and Dibenzoyl with Dimethylhydrazine. N. A. Domnin, V. I. Diurnbaum, and V. A. Cherkasova	1520	1469
Investigation of Transformations of Pinacols with Substituted Acetylenic Radicals. XVI. Synthesis and Transformations of Sym. Dimethylphenyl(tertbutylethynyl) Ethylene Glycol (3,6,6-Trimethyl-2-phenylheptyn-4-diol-2,3). E. D. Venus-Danilova and V. I. Serkova	1528	1477
Investigations in the Pyrimidine Series. Action of Hydrogen Peroxide on Mercapto-pyrimidines. Formation of Pyrimidine Sulfones and Their Instability in the Presence of Hydrogen Peroxide. Ch'ih Yueh-fon and Ch'en Shu-feng	1533	1483
Investigations in the Thiazole Series. V. Synthesis of 2-δ-Amino-n-butyl-4-N-diethylaminomethylthiazole. Ch'ih Yueh-fon and Zin Shih-yung	1542	1492
An Anomalous Reaction of α-Halo Ketones with Esters of Phosphorous Acid. VII. Reactions of Esters of Phosphorous Acid with Chlorinated Derivatives of β-Diketones. A. N. Pudovik and L. G. Biktimirova	1545	1496
The Problem of the Bromination of Cyclic Ketones with Dioxane Dibromide. L. V. Machinskaia and A. S. Podberezina	1550	1501

CONTENTS (continued)

	PAGE	RUSS. PAGE
5-Chlorofurylnitroolefins. Z. N. Nazarova and F. T. Pozharskii	1553	1503
Synthesis of Thiazolidone Derivatives of Biological Interest. IX. Synthesis of 3-Derivatives of 2,4-Thiazolidinedione Hydrazone. E. V. Vladzimirskaia	1555	1505
Interaction of β-Chlorovinyl Ketones with β-Dicarbonyl Compounds. V. Ketovinylation of α-Alkyl Acetoacetic Esters. N. K. Kochetkov, B. P. Gottikh and L. I. Kudriashov	1559	1508
Interaction of β-Chlorovinyl Ketone with β-Dicarbonyl Compounds. VI. Synthesis of some Derivatives of α-Pyrones. N. K. Kochetkov and L. I. Kudriashov	1562	1511
Synthesis and Properties of Pyrrolidine Bases. IV. 2-Methyl-N-β-aminoethylpyrrolidine and some of Its Transformations. A. P. Terent'ev, M. A. Volodina and V. G. Mishina	1566	1516
4-Nitro-1,3-indanedione. G. Ia. Vanag and V. P. Oshkaia	1570	1520
Synthesis and Polycondensation of N-Alkyl Derivatives of Hexamethylenediamine. III. Influence of the Structure of the Substituting Radical on the Direction of Alkylation of Hexamethylenediamine. A. L. Klebanskii and M. S. Vilesova	1574	1524
Synthesis of N-Alkyl Derivatives of Hexamethylendiamine and Their Polycondensation. V. Some Problems of the Kinetics of the Reductive Alkylation of Hexamethylenediamine. A. L. Klebanskii and M. S. Vilesova	1578	1528
The Fermentative Synthesis of N-Peptides from O-Peptides of β-Hydroxyamino Acids. M. M. Botvinik and S. M. Avaeva	1583	1534
Investigation of the Exchange Reaction of Oxy Radicals with Radicals of Organomagnesium Compounds. III. Interaction of Organomagnesium Compounds with Mixed Organosilicon Acetals. M. F. Shostakovskii, M. R. Kulibekov, and I. A. Shikhiev	1588	1539
Synthesis and Transformations of Butadienylsilanes. S. I. Sadykh-zade and A. D. Petrov	1591	1542
Reactions of Magnesylamines. VI. Steric Hindrance in the Aramidation of Aromatic Aldehydes with the Help of N,N'-bis-(halomagnesium)arylamines. P. A. Petiunin and L. A. Tetiueva	1596	1548
Synthesis of Organophosphorus Compounds from Hydrocarbons and Their Derivatives. VII. Oxidative Chlorophosphonation by Means of Alkyl and Dialkylamidophosphorodichloridites. Iu. M. Zinov'ev, V. N. Kulakova and L. Z. Soborovskii	1600	1551
Tetraacyloxysilanes in Organic Synthesis. XV. Synthesis of α,β-Unsaturated Acids of the Furan and Thiophene Series. Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov	1603	1554
The Chlorination of n-Hexane and n-Heptane. V. A. Nekrasova	1606	1557
The Problem of the Production of Aliphatic Alcohols from Petroleum Hydrocarbons. V. A. Nekrasova	1610	1561
Reaction of Dialkyl Dithiophosphates with Ethylene Sulfide. T. A. Mastriukova, V. N. Odnoralova and M. I. Kabachnik	1613	1563

CONTENTS (continued)

	PAGE	RUSS. PAGE
Organophosphorus Insecticides. Some Derivatives of Methylthiophosphonic and Methyldithiophosphonic Acids. M. I. Kabachnik, N. N. Godovikov, D. M. Paikin, M. P. Shabanova, N. M. Gamper and L. F. Efimova	1618	1568
An Investigation in the Field of Alkanesulfonic Acids. XVI. Chlorination of Anisidides of Alkanesulfonic Acids. A. G. Kostsova	1623	1573
Investigations in the Field of Quinoline Derivatives. XIX. A New Method of Synthesis of Quinolines by Rearrangement of Acylated Arylamines. B. I. Ardashev and V. I. Minkin	1627	1578
Interaction of Aqueous Solutions of Salts of Tetravalent Titanium with Pyrazolone Derivatives. R. G. Beiles	1631	1581
Anilides of Alkylsulfonamidophosphoric Acids. A. V. Kirsanov and N. L. Egorova.	1636	1587
Salts of the Acid Fluorides of Arylsulfonamidophosphoric Acids. A. V. Kirsanov and E. S. Levchenko	1639	1589
Diphenylamides of Trichlorophosphazocarbonic Acids and Their Derivatives. A. V. Kirsanov and Z. D. Nekrasova	1644	1595
2,4-Di-(ethyleneimino)-1,3,5-triazines. L. E. Sventsitskaia, A. A. Kropacheva and S. I. Sergievskaia	1650	1601
Synthesis of p-Nitrophenylhalogenomethyl Carbinols. L. M. Iagupol'skii, B. E. Gruz and A. I. Kiprianov	1656	1608
Absorption spectra and Structure of the Bisulfite Compound of Acridine. V. I. Blizniukov and A. K. Sukhomlinov	1659	1610
Absorption Spectra and Structure of 2-Methoxyaminoacridine-9. V. I. Blizniukov and A. K. Sukhomlinov	1662	1613
Synthesis of Phosphoramidopyrimidines. Iu. P. Shvachkin and M. A. Prokof'ev	1665	1617
Chloromethylation of Saturated α,ω-Phenylaliphatic Acids. M. N. Bogdanov	1670	1621
Organozinc Compounds as Catalysts in the Polymerization of Propylene. G. A. Razuvaev, L. M. Bobinova, and V. S. Emlis	1672	1623
Condensation of Diacetone Alcohol with Benzene. I. P. Labynskii	1676	1626
Synthesis of Organophosphorus Compounds from Hydrocarbons and Their Derivatives. VIII. A Study of Oxidation of Phosphorus Trichloride by Oxygen. M. K. Baranaev, Iu. M. Zinov'ev, T. K. Skripach and L. Z. Soborovskii	1678	1628
Reactions of Free Radicals in Solution. XIV. Formation of Free Radicals in Decomposition of Hydrogen Disulfide and Their Reactions with α- and β-Olefins. E. I. Tiniakova, E. K. Khrennikova and B. A. Dolgoplosk	1682	1632
Orientation in Aromatic Ring Substitution. III. Isomerization of Dichlorobenzenes. A. A. Spryskov and Iu. G. Erykalov	1688	1637
The Study of Sulfonation Reaction. XLVII. The Study of Chlorobenzenesulfonic Acid Hydrolysis with the Use of Radioactive Indicators. A. A. Spryskov and O. I. Kachurin	1693	1642

CONTENTS (continued)

	PAGE	RUSS. PAGE
Mechanism of α-Tetraloxime Conversion into α-Naphthylamine. N. N. Vorozhtsov and V. A. Koptiug	1697	1646
The Problem of the Reduction of 1-Methyl-1-cyclohexene Oxide. G. V. Pigulevskii. S. A. Kozhin, and V. G. Kostenko	1706	1656
The Formation of 5-Benzylhydantoin-3-acetylvaline from the Methyl Ester of N-Carbobenzoxyphenylalanylglycylvaline. E. A. Morozova and S. M. Zhenodarova	1708	1658
The Synthesis of Cyanomethyl Esters of Peptides and Their Use in Obtaining Peptides. E. A. Morozova and S. M. Zhenodarova	1711	1661
Studies in the Field of the Chemistry of the Cyanine Dyes. XIII. Thiacyanines which Contain Unsaturated Radicals as Substituents in the 6,6'-Positions of Benzthiazole I. K. Ushenko and S. E. Gornostaeva	1717	1668
Monoanils of Glutaconic Aldehyde. I. Derivatives of Primary Aromatic Amines. N. E. Grigor'eva and A. A. Pechka	1726	1677
Monoanils of Glutaconic Aldehyde. II. Effect of the Medium on the Color of Derivatives of Primary Aromatic Amines. N. E. Grigor'eva and I. K. Gintse	1730	1682
Investigation of Anode Deposits Formed in the Electrolysis of Solutions of Certain Thallium Salts. III. M. S. Skanavi-Grigor'eva and V. I. Staroverova	1737	1689
Irreversible-Common System of Sodium and Potassium Butyrates and Thiocyanates. N. M. Sokolov and E. I. Pochtakova	1741	1693
Toward the Question of Contact Fusion of Crystals. P. A. Savintsev and V. E. Avericheva	1748	1700
Investigation of the Reaction of Phenyl-β-naphthylamine with Organic Acids by the Methods of Physicochemical Analysis. N. K. Tsvetkova and D. E. Dionis'ev	1750	1702
Compounds of Cadmium and Mercury Halides with Nicotine. I. A. Kondrashov and S. F. Babak	1753	1705
Letters to the Editor		
Study of the Wallach Rearrangement and Related Reactions. M. M. Shemiakin, V. I. Maimind and B. K. Vaichunaite	1756	1708
Synthesis of L-Acetylalanine from D,L-Alanine. V. P. Spirichev and L. A. Shchukina	1758	1709

DIENE HYDROCARBONS FROM UNSATURATED ALCOHOLS

II. CATALYTIC DEHYDRATION OF TIGLYL ALCOHOL* AND 2-ETHYLHEXEN-2-OL-1 TO DIENE HYDROCARBONS

Iu. A. Gorin, V. S. Ivanov and E. K. Khrennikova

As we established previously [1], the use of one of the components of Lebedev's catalyst (B_2) and a phosphate catalyst as a dehydrating catalyst makes it possible to prepare divinyl from crotyl alcohol in high yield (up to 88.5%, calculated on the alcohol passed). It appeared interesting to examine the possibility of using these catalysts for the dehydration of other α,β-unsaturated alcohols in order to obtain from them hydrocarbons with a conjugated system of double bonds. We tested the effect of these catalysts on tiglyl alcohol and 2-ethylhexen-2-ol-1.

D. V. Tishchenko has shown [2,3] that tiglyl alcohol, like the secondary alcohol, isopropenylmethylcarbinol, which is isomeric to it, or a mixture of them, is dehydrated over anhydrous magnesium sulfate at 230-260° to isoprene in a yield of 60% on the alcohol passed and 85-90% on the alcohol reacted. In the present work we show that under the action of one of the dehydration components of Lebedev's catalyst (B_2) and a phosphate catalyst (PH)**[1] tiglyl alcohol may give a yield of isoprene representing 67% of the alcohol passed. Dilution of the starting alcohol vapor with nitrogen did not increase the isoprene yield.

2-Ethylhexen-2-ol-1 may be considered as the intermediate product of the catalytic conversion of n-butyl alcohol to a C_8 diene hydrocarbon over Lebedev's catalyst [4]. As the present work established, dehydration of 2-ethylhexen-2-ol-1 gave a mixture of diene hydrocarbons with 8 C-atoms, which contained 2-ethylhexadiene-1,3 and also, possibly, 3-methylheptadiene-3,5. 2-Ethylhexadiene-1,3 was the primary dehydration product. We assume that under the effect of high temperature and the catalyst it was partly isomerized into 3-methylheptadiene-3,5. This hypothesis agrees with the data given by Prevost [5], who showed that dehydration of vinylpropylcarbinol over aluminum oxide at 340°C gave a mixture of hexadiene-1,3 and hexadiene-2,4. The total yields of C_8H_{14} hydrocarbons, prepared by dehydrating the unsaturated alcohol $C_8H_{15}OH$ over the catalysts mentioned above, were 87-95% of the alcohol reacted.

According to I. I. Ostromyslenskii's ideas [6], catalytic dehydration of crotyl alcohol over aluminum oxide proceeds with the intermediate formation of methylallene which then is isomerized to divinyl.

$$CH_3{-}CH{=}CH{-}CH_2OH \xrightarrow{-H_2O} CH_3{-}CH{=}C{=}CH_2 \rightarrow CH_2{=}CH{-}CH{=}CH_2$$

In contrast to Ostromyslenskii, Prevost [7] considers that when dehydrated over aluminum oxide, crotyl alcohol is first isomerized to methylvinylcarbinol which then splits out the elements of water to form divinyl.

$$CH_3{-}CH{=}CH{-}CH_2OH \rightarrow CH_3{-}CHOH{-}CH{=}CH_2 \xrightarrow{-H_2O} CH_2{=}CH{-}CH{=}CH_2$$

Prevost also considers the possibility that water was eliminated from the carbon atoms in the 1,4 positions followed by closing of the bonds.

$$CH_3{-}CH{=}CH{-}CH_2OH \xrightarrow{-H_2O} {-}CH_2{-}CH{=}CH{-}CH_2{-} \rightarrow CH_2{=}CH{-}CH{=}CH_2$$

* 2-Methylbuten-2-ol-1.

** Used in Germany in the synthetic rubber industry for the dehydration of butylene glycol-1,3 to divinyl [12].

According to the data given by D. V. Tishchenko [2], who obtained isoprene by dehydrating tiglyl alcohol, and according to data from the present work, when dehydrated catalytically, α,β-unsaturated alcohols of the type $R' - CH_2 - CH = C(R) - CH_2OH$, where R is an alkyl radical and R' hydrogen or an alkyl radical, form hydrocarbons with a conjugated system of double bonds. It follows from this that the reaction cannot proceed through the intermediate stage of the formation of the allene grouping as the α-carbon atom lacks the hydrogen required for this. As the elimination of water from crotyl alcohol and from α,β-unsaturated alcohols which have a substitutent alkyl group (methyl or ethyl) in the α-position must proceed according to the same mechanism, then Ostromyslenskii's hypothesis cannot be considered as realistic. The problem of whether the allyl rearrangement occurs before dehydration or whether the elements of water are eliminated directly from the 1,4 position, remains unclear and requires further study.

EXPERIMENTAL

1. Dehydration of tiglyl alcohol. The tiglyl alcohol was obtained by the reduction of tiglaldehyde by the Meerwein-Ponndorf method [8-10]. The tiglaldehyde was obtained by a mixed aldol condensation of acetaldehyde and propionaldehyde in ether in the presence of aqueous alkali [11]. The yield of tiglyl alcohol was 40% of theoretical. The tiglyl alcohol obtained distilled at 135-140° and was characterized by the following constants:

b.p. 135-137°, d_4^{17} 0.8671, d_4^{20} 0.8655, n_D^{20} 1.4420; b.p. 137-140°, d_4^{17} 0.8668, d_4^{20} 0.8653, n_D^{20} 1.4429. According to literature data for tiglyl alcohol: b.p. 136-137°, d_4^{17} 0.8672; b.p. 137-139°, d_4^{17} 0.8667 [2], n_D^{20} 1.4420 [9].

The tiglyl alcohol was dehydrated in the small vertical laboratory furnace, which we described previously [1]. The volume of catalyst was 18 ml. During an experiment, 4-5 ml of alcohol who passed through the furnace. The reaction products were condensed in a condenser and collected in a receiver, cooled with a mixture of ice and salt. Practically no gas formation was observed. Data from the experiments are presented in Table 1.

The isoprene was evaporated off from the condensate in a stream of nitrogen at 60° and passed into a gasometer. The isoprene content of the mixture of nitrogen and isoprene vapor obtained was determined on a sample using maleic anhydride [13]. The gaseous mixture of nitrogen and isoprene was passed through a trap at −60°, into which the isoprene condensed. The portions of isoprene obtained in different experiments were

TABLE 1

Catalytic Dehydration of Tiglyl Alcohol into Isoprene

Experiment No.	Catalyst	Temperature of experiment	Input rate (ml/hr/ml of catalyst)	Amount of alcohol passed (in g)	Wt. of isoprene obtained (in g)	Yield of isoprene on alcohol passed (in %)
1	B_2	325°	1.31	4.33	1.82	59.1
2	B_2	325	0.56	4.33	2.08	67.6
3	B_2	350	0.61	4.33	1.95	63.4
4	B_2	375	0.26	4.33	1.32	42.9
5*	B_2	350	0.63	3.46	1.64	66.8
6	Ph	280	0.23	3.46	1.66	67.5

* Diluent – nitrogen, degree of dilution – 1:3 (mole).

combined and distilled from a flask with a Vigreux distillation column. The distillation yielded a product with b.p. 34.4°, d_4^{20} 0.6808, n_D^{20} 1.4191. According to literature data for isoprene: b.p. 34.5-35°, d_4^{20} 0.6806, n_D^{20} 1.4194 [14]. The adduct obtained from the isoprene and maleic anhydride had m.p. 63°. According to literature data, m.p. 63 – 64° [15].

2. Dehydration of 2-ethylhexen-2-ol-1. n-Butyraldehyde was used as the starting material for the preparation of 2-ethylhexen-2-ol-1. It was condensed in the presence of NaOH [16] to give 2-ethylhexen-2-al-1.

The yield of the doubly distilled product was 83%: it had b.p. 168-169°, d_4^{20} 0.8506, n_D^{20} 1.4519. The unsaturated aldehyde obtained was reduced to the corresponding alcohol with aluminum isopropoxide by a procedure similar to that used for the preparation of crotyl and tiglyl alcohols. A second distillation yielded a main fraction with b.p. 179-180° (yield 51.5%), d_4^{20} 0.8568, n_D^{20} 1.45079.

Found %: OH 13.47. Hydrogen number 151. $C_8H_{15}OH$. Calculated %: OH 13.26. Hydrogen number 157.

The α-naphthylurethan was recrystallized from dioxane to give white needles with m.p. 75.5-76.0°.

Found %: N 4.61. $C_{19}H_{23}O_2N$. Calculated %: N 4.71.

The dehydration of 2-ethylhexen-2-ol-1 (see Table 2) was carried out with the apparatus and the catalysts described above. During an experiment 20-50 ml of alcohol was passed.

TABLE 2

Catalytic Dehydration of 2-ethylhexen-2-ol-1

Expt. No.	Catalyst	Temp. of expt.	Input rate (ml/hr/ml of catalyst)	Am't of alcohol passed (in g)	Wt. of hydrocarbons obtained (g)	Amt. of alcohol reacted (in %)	Yield of C_8H_{14} (in %) on	
							alcohol passed	alcohol reacted
1	Ph	280°	0.33	42.90	29.78	84.8	80.7	95.1
2**	Ph	280	0.28	17.16	7.52	60.6	51.0	89.5
3	B_2	350	1.00	42.90	25.70	76.6	69.9	90.7
4	B_2	350	2.10	17.16	9.65	74.1	65.4	88.2

* Diluent – water, degree of dilution – 1 : 12 (mole).

The hydrocarbons were isolated from the upper layer of the condensate. They were separated from alcohols, either by converting the latter to alcoholates or by converting them to boric esters [17] and then distilling them off from the hydrocarbons.

a) Investigation of hydrocarbons obtained on the phosphate catalyst. 27.87 g of the hydrocarbons was separated into fractions (weight percents are given) by distillation: 1st 120-128°, 10.9%, n_D^{20} 1.4534; 2nd, 128-130°, 3.6%, n_D^{20} 1.4579; 3rd, 130-132°, 13.9%, n_D^{20} 1.4619; 4th, 132-134°, 28.2%, n_D^{20} 1.4667; 5th, 134-135.5°, 28.7%, n_D^{20} 1.4688; residue 12.8%, n_D^{20} 1.4651; losses 1.9%.

The 5th fraction with b.p. 134-135.5° was investigated in detail; it was redistilled over the same range:

d_4^{20} 0.7634, n_D^{20} 1.4694, MR_D 40.23; found 38.21, EMR_D 2.02.
Found %: C 87.03; H 12.82. M 110.4. C_8H_{14}. Calculated %: C 87.27; H 12.72. M 110.19.

There is no literature data for 2-ethylhexadiene-1,3; for 3-methylheptadiene-3,5 [18]: b.p. 135.2°, d_4^{20} 0.7652, n_D^{20} 1.4693.

The 5th fraction was hydrogenated in alcohol in the presence of platinum black. The amount of hydrogen added corresponded to 2 moles of hydrogen per mole of diene hydrocarbon. The hydrogenation product was identified as 3-methylheptane:

b.p. 117.5°, d_4^{20} 0.7063, n_D^{20} 1.39885.
Found %: C 84.31; H 16.17. C_8H_{18}. Calculated %: C 84.11; H 15.89.

Literature data for 3-methylheptane: b.p. 118.93°, d_4^{20} 0.7058, n_D^{20} 1.3985 [19].

When treated with a saturated SO_2 solution, samples of fractions 4 and 5 formed white amorphous precipitates of polymeric sulfone.

Treatment of the 5th fraction with maleic anhydride with heating on a water bath and also at room temperature gave a polymeric product. In toluene at –20°, the reaction led to the formation of a crystalline derivative with m. p. 62° (from ligroin) and a small portion of insoluble (polymeric) product.

Treatment of the 5th fraction with α-naphthoquinone under the conditions described by B. A. Arbuzov and V. S. Abramov [20] led to the formation of an adduct, which appeared as grey scales with m.p. 121° Dehydrogenation of this yielded a tetrahydroanthraquinone derivative – a grey-violet substance, which did not melt at 360°. Oxidation of the latter by Elbs' method [21] gave a finely crystalline substance with a yellow color which did not melt at 350°.

Literature data: for anthraquinonemonocarboxylic acid, m.p. 285-286° [20]; 1,3-anthraquinonedicarboxylic acid does not melt up to 330° [22]; 1,2,4-anthraquinonetricarboxylic acid does not melt up to 320° [23] or decompose at 320° [24].

Found: equiv. 143 (titration in alcohol solution). $C_{14}H_6O_2(COOH)_2$. Calculated: equiv. 148.

The 5th fraction was ozonized in ethyl chloride solution at –70° by the method developed by A. I. Iakubchik [25] for the determination of the vinyl groups in synthetic rubbers. The ozonide was decomposed with hot water and the formic acid in the ozonolysis products determined by the calomel method [26] and the formaldehyde by precipitation with β-naphthol [27]. Found: 63.4% of the hydrocarbon C_8H_{14} had double bonds at the end of the chain (i.e. $>$ $C=CH_2$-groups).

The results of ozonization and the data obtained from oxidation of the dehydrogenated condensation product of the hydrocarbon and α-naphthoquinone (formation of anthraquinone dicarboxylic acid) indicates that the fraction contained 2-ethylhexadiene-1,3, $CH_3CH_2CH=CH-C(C_2H_5)=CH_2$, with b.p. 134-135.5°, which was the primary dehydration product of 2-ethylhexen-2-ol-1. However, the presence of polymeric product in the adduct, obtained by condensing the hydrocarbon fraction examined with maleic anhydride, and also data on the boiling point, density, refractive index and the ozonization results indicate that the fraction also contained 3-methylheptadiene-3,5. In the literature there is a report [28, 29] that α,α-substituted diene hydrocarbons will condense with maleic anhydride to give polymeric products.

b) Investigation of hydrocarbons obtained on catalyst B_2. 25.7 g of the hydrocarbons was distilled to give the following fractions: 1st, 108.5-121.5°, 5.9%, n_D^{20} 1.4369; 2nd, 121.5-129.5°, 24.3%, n_D^{20} 1.4502; 3rd, 129.5-132.5°, 10.7%, n_D^{20} 1.4602; 4th, 132.5-134.0°, 17.2%, n_D^{20} 1.4658; 5th, 134.0-135.5°, 29.6%, n_D^{20} 1.4682; residue 9.8%, n_D^{20} 1.4682; losses 2.3%. The fraction with b.p. 134-135.5° was redistilled over the same range: d_4^{20} 0.7614, n_D^{20} 1.4687.

The combined fractions with b.p. 129.5-135.5° were hydrogenated as described above. The amount of hydrogen added corresponded to 2 moles per mole of C_8H_{14} hydrocarbon. The hydrogenation product isolated was identified as 3-methylheptane:

b.p. 117.8°, d_4^{20} 0.7066, n_D^{20} 1.3982.

Found %: C 83.80; H 15.76. C_8H_{18}. Calculated %: C 84.11; H 15.89.

Treatment of samples of fractions 3, 4, and 5 with a saturated solution of SO_2 gave white amorphous tablets of a polymeric sulfone. Samples of fractions 1 and 2 gave turbidity but no precipitate.

Treatment of the 5th fraction with maleic anhydride, as described above for experiments on the phosphate catalyst, gave a crystalline product only for condensations in toluene solution at –20° (white needles from ligroin, m.p. 61.5-62°). A mixed melting point with the product obtained from the hydrocarbon in experiments with the phosphate catalyst was not depressed.

Under the same condensation conditions, the hydrocarbon of fraction 4 gave a gelatinous, polymeric mass.

Treatment of the 5th fraction with α-naphthoquinone under the conditions described above, gave a condensation product – dark red needles with m.p. 121.5°. A mixed sample with the analogous product prepared from the hydrocarbon obtained on the phosphate catalyst, melted at 121.0°.

We would like to thank N. G. Kasatkina, who helped us with the ozonization of the hydrocarbon.

SUMMARY

1. The catalytic dehydration of tiglyl alcohol to isoprene on one of the dehydrating components of Lebedev's catalyst (B_2) and a phosphate catalyst, used for the industrial production of divinyl from butylene glycol-1,3 was investigated. The yield of isoprene on the above catalysts represented 67% of the tiglyl alcohol passed.

2. Catalytic dehydration of 2-ethylhexen-2-ol-1 over the same catalysts was investigated. The hydrocarbon yield (calculating on C_8H_{14}) was 80% of alcohol passed and 95% of that reacted over the phosphate catalyst and 70% of alcohol passed and 90% of that reacted over catalyst B_2. It was shown that the C_8H_{14} hydrocarbons prepared on the two catalysts were identical and that they consisted mainly of 2-ethylhexadiene-1,3, which was the primary dehydration product.

3. As the catalytic dehydration of crotyl alcohol and of α,β-unsaturated alcohols, with an alkyl group in the α-position, to form conjugated dienes probably proceed by the same mechanism, Ostromyslenskii's hypothesis that a compound with an allene grouping may be formed as an intermediate stage should be considered groundless.

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INVESTIGATION OF CONJUGATED SYSTEMS

LXXXVII.* ADDITION OF α-CHLORO- AND α-BROMO-ETHERS TO CHLOROPRENE

B. A. Vovsi and A. A. Petrov

The addition of halogen derivatives to diene compounds has been studied on very few examples [1]. The order of addition of α-chloro-ethers to divinyl has been investigated quite thoroughly [2, 3]. B. A. Arbuzov and A. N. Pudovik estiblished that in the case of divinyl, mostly 1,2-products are formed; however, the addition catalyst ($ZnCl_2$) induced isomerization of the latter to 1,4-products, which predominate in the final reaction mixture. The yield of alkoxychloroisohexenes was low (30-37%) on reacting α-chloro-ethers with isoprene (mainly 1, 4-addition) [4]. The decrease in the yield of the primary addition products (in a ratio of 1 : 1) is due to the fact that in the case of isoprene these products have a stronger tendency for telomerization than in the case of divinyl [5].

There are also data on the order of addition of alkyl halides to divinyl and isoprene and of polyhalomethanes and ethanes to divinyl [1, 5]. The addition of α-halo-ethers to diene halogen derivatives has not been studied.

We decided to establish the order of addition of α-chloro- and α-bromo-ethers to chloroprene. As a result of reacting chloroprene with α-halo-ethers one might expect the formation of the following six isomers:

$CH_2Cl-CCl(CH_2OR)-CH=CH_2$ (I), $CH_2=CCl-CHCl-CH_2-CH_2OR$ (IV),
$CH_2OR-CH_2-CCl_2-CH=CH_2$ (II), $CH_2Cl-CCl=CH-CH_2-CH_2OR$ (V),
$CH_2=CCl-CH(CH_2OR)-CH_2Cl$ (III), $CH_2OR-CH_2-CCl=CH-CH_2Cl$ (VI).

The substances actually obtained boiled over a narrow temperature range. Their constants are given in Table 1.

TABLE 1

$CH_2OR-CH_2-CCl=CH-CH_2Hlg$		Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Hlg (%)		Yield (in %)
R	Hlg				found	calc.	found	calc.	
CH_3	Cl	48.9—49.1° (2) 79.5—81 (10)	1.1613	1.4770	41.05	40.82	41.48	41.95	53
C_2H_5	Cl	55.8—56° (2) 86.6—87.4 (10)	1.1156	1.4724	45.94	45.44	38.11	38.73	67
C_3H_7	Cl	68.9—69.1 (2)	1.0901	1.4700	50.40	50.05	36.21	35.98	63
C_3H_7-iso	Cl	60.2—60.3 (2)	1.0831	1.4660	50.45	50.05	35.75	35.98	64
CH_3	Br	72.5—73 (5)	1.4297	1.5070	44.44	43.72	54.33	54.04	70
C_2H_5	Br	85.3—86.1 (5)	1.3539	1.4998	49.41	48.33	51.06	50.76	78
C_3H_7	Br	76.5—77.5 (2)	1.3075	1.4922	53.61	52.95	47.64	47.77	49
C_3H_7-iso	Br	68 —68.2 (2)	1.2984	1.4900	53.78	52.95	48.18	47.77	50

*Diene compounds, LXVI. Reactions of dienes with halogen derivatives. III.

The data in Table 1 show that over the series of chloro- and bromo-ethers there is a regularity in the increase in boiling points and the decrease in specific gravities and refractive indexes. A molecular refraction greater than that calculated was found for all the ethers, with a difference of 0.4 in the chloro-ether series and 0.7-1 in the bromo-ether series. This phenomenon has been observed several times in the case of materials with similar structures.

TABLE 2

Substance	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Found (%) C	H	Cl	N	OR	Calculated (%) C	H	Cl	N	OR
$CH_3OCH_2—CH_2—CCl{=}CH—CH_2OCH_3$	53.5—53.6° (2) 77—78.6 (10)	1.0622	1.4572	42.23	42.21	46.96, 49.61	8.04, 7.65	— —	— —	37.80, 37.20	51.07	7.96	21.54	—	37.70
$C_2H_5OCH_2—CH_2—CCl{=}CH—CH_2OC_2H_5$	66.5—67 (2) 92—94 (10)	1.0239	1.4552	51.08	51.45	55.31, 54.40	8.89, 8.88	18.63, 18.79	— —	45.05, 46.80	56.10	8.89	18.41	—	46.77
$CH_3OCH_2—CH_2—CCl{=}CH—CH_2N(C_2H_5)_2$	88.5—89 (5) 102—103.5 (10)	0.9684	1.4610	58.30	58.03	59.64, 59.36	9.69, 9.80	16.93, 16.80	6.71, 6.80	—	58.37	9.80	17.24	6.81	—
$C_2H_5OCH_2—CH_2—CCl{=}CH—CH_2N(C_2H_5)_2$	100.5—103 (5) 109.2—111.5 (10)	0.9514	1.4569	62.90	62.64	60.57, 60.54	10.10, 10.07	15.38, 15.28	6.40, 6.47	— —	60.61	10.09	16.14	6.37	—

The structure of the reaction products of α-halo-ethers and chloroprene was established from data on their selective ozonization, reduction and dehalogenation with alcoholic alkali.

1. Decomposition of the ozonides of the addition products of chloroprene and α-chloromethyl ethyl ether gave β-ethoxypropionic acid and a smaller amount of chloroacetic acid. The reaction products also contained chloroacetaldehyde (determined as the 2,4-dinitrophenylhydrazone) but no ethoxypropionaldehyde. These data indicate that the substance has a 1,4-structure and most probably formula (VI).

2. The 1,4-structure of the addition products of α-chloro- and α-bromo-ethers and chloroprene is also supported by experiments on determining primary allyl chlorine in them, by the Sommelet-Leets method [6, 7]. The reaction proceeded very slowly in this case although in two days it was 90-95% complete.

3. Formula (VI) is supported by experiments on the effect of zinc dust in an aqueous-alcohol medium on the addition products of α-chloromethyl and α-chloromethyl ethyl ethers. This gave only small amounts of liquids with low boiling points, which, judging by the infrared spectra, either contain none or very minute quantities of allene ethers which are the probable reduction products of substances with formula (V).

4. According to formula (VI) the addition products of α-halo-ethers and chloroprene very readily exchange one of the halogen atoms for a hydroxyl, ether or amino group. When treated with alcoholic alkali in the cold they gave a series of diethers of an unsaturated, chlorine-containing glycol and when treated with diethylamine— the corresponding ethers of diethylaminochloropentenol. The constants of these substances are given in Table 2.

It was thus established that the addition of α-halo-ethers occurred exclusively or almost exclusively in accordance with the assumed polarization of the chloroprene molecule in the 1,4-position.

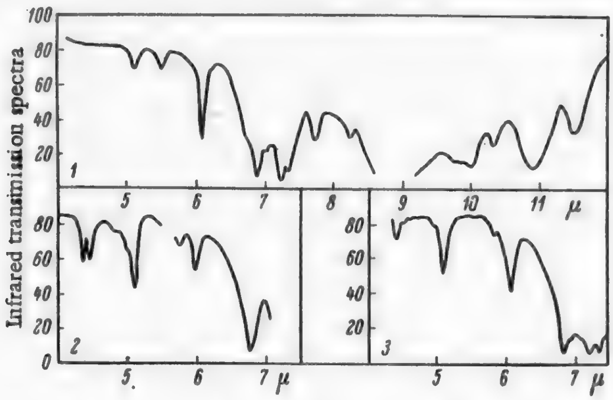
Heating diethers of chloroglycol and ethers of diethylaminopentenol with solutions of KOH in Cellosolve eliminated hydrogen halide to form a mixture of acetylene, allene and diene compounds. This structure for the dehalogenation products is based on a study of their infrared spectra (figure); in them we detected frequencies characteristic of an acetylene bond (4.42μ) and an allene (5.09μ) and a 1,3-diene (5.97-6.04μ) system. These mixtures were not studied in greater detail.

The α-chloro- and α-bromo-ethers were prepared by the action of gaseous hydrogen halides on a suspension of paraformaldehyde in the appropriate alcohol and were purified by distillation

at normal pressure. The yields were 60-80% (on paraformaldehyde).

The properties of the α-chloro- and α-bromo-ethers we prepared are given in Table 3. Ethers 4, 6, 10-12 are described for the first time. The boiling points of the rest agreed with literature data.

The α-halo-ethers were reacted with chloroprene in a liter, four-necked, round-bottomed flask, fitted with a reflux condenser, a thermometer, a dropping funnel and a stirrer with divergent paddles. Stirring was



Infrared transmission spectra. 1) Low-boiling fraction, formed by the action of zinc dust on the product of adding chloromethyl ethyl ether, 2) substance formed by heating the product of adding chloromethyl methyl ether with KOH in Cellosolve, 3) substance formed under the same conditions from the unsaturated diethylaminochloro-ether (R = CH_3).

maintained at such a rate that the reading on the thermometer in the flask with the reaction mixture, rapidly reached the reading of a thermometer in the bath cooling the flask. Into the flask was placed zinc chloride or bromide (0.2 g) and then a mixture of 0.5 mole of chloroprene and 0.5 mole of α-halo-ether was added. The reaction mixture, which was first cooled to 0°, was gradually heated to room temperature. The beginning of the reaction was characterized by the appearance of a color at the point of contact with the catalyst and a rise in temperature. The latter was kept at 40-50° by external cooling. At the end of the exothermic process, the mixture was heated for half an hour at 65-70°. The absence of condensate dripping from the reflux condenser, indicated the end of the reaction. Then the contents of the flask were diluted with ether. The ether solution was washed with water containing ammonium oxalate (for the most efficient removal of the catalyst), dried with potash and distilled. The constants, yields and analytical data for the substances obtained are given in Table 1.

TABLE 3

Expt. No.	Substance	Boiling point	Yield (in %)
1	$CH_2Cl—OCH_3$	59.5—60°	82
2	$CH_2Cl—OC_2H_5$	81.9—82	81
3	$CH_2Cl—OC_3H_7$	108.5—109.5	75
4	$CH_2Cl—OC_3H_7$-iso	101.6—101.7	58
5	$CH_2Cl—OC_4H_9$	132—134	78
6	$CH_2Cl—OC_4H_9$-iso	122—124	75
7	$CH_2Br—OCH_3$	87.3—88	79
8	$CH_2Br—OC_2H_5$	109.1—109.9	80
9	$CH_2Br—OC_4H_7$	132—134	75
10	$CH_2Br—OC_3H_7$-iso	122.2—122.6	67
11	$CH_2Br—OC_4H_9$ iso	154.3—156.0	77
12	$CH_2Br—OC_4H_9$-iso	144.4—146.2	76

Ozonization. The product of adding chloromethyl ethyl ether to chloroprene (10.44 g) was ozonized in ethyl chloride. The ozonide was decomposed with water at a temperature of 80°. The solution was neutralized with sodium bicarbonate and freed from aldehydes by partial distillation in vacuum. The residue was acidified with 2 N sulfuric acid and extracted with ether. After removal of the ether, the acids were fractionated at 10 mm. Two fractions were collected - 1st with b.p. 96-98°, 2.5 g; 2nd with b.p. 98-106°, 4.2 g.

The first fraction was found to contain chloroacetic acid, which was isolated as phenoxyacetic acid (0.12 g, which corresponded to 0.075 g of chloroacetic acid). The m.p. was 98° and a mixed sample melted at 98° [8].

A second distillation of the 2nd fraction yielded a product with b.p. 118-120° (20 mm), which contained about 85% of ethoxypropionic acid, together with chloroacetic acid, which was obvious from the analysis data.

Found %: C . 47.57, 47.69; H 7.78, 7.84; OC_2H_5 33.1, 33.9. $C_5H_{10}O_3$. Calculated %: C 50.83; H 8.53; OC_2H_5 38.14. $C_2H_3O_2Cl$. Calculated %: C 25.42; H 3.20.

The aldehydes contained in the distillate were treated with a hydrochloric acid solution of 2,4-dinitrophenylhydrazine. We obtained 0.51 g of the 2,4-dinitrophenylhydrazone of chloroacetaldehyde.

Found %: N 21.42, 22.01; Cl 13.70, 13.85. $C_8H_7O_4N_4Cl$. Calculated %: N 21.66; Cl 13.71.

TABLE 4

$RO-CH_2-CH_2-CCl=CH-CH_2Hlg$		Yield of primary chloride (in %)	
R	Hlg	after 3.5 hrs	after 50 hrs
CH_3	Cl	79.49	85.80
CH_3	Br	97.20	—
C_2H_5	Cl	96.04	97.26
C_3H_7	Cl	87.23	99.02
C_3H_7	Br	84.55	97.88
C_3H_7- iso	Cl	86.24	101.14
C_3H_7- iso	Br	91.27	92.43

Reaction with urotropine [7]. Samples of the ethers (0.5-1.0 g) were added to an acetone solution of potassium iodide and then shaken with urotropine for 3.5 and 50 hours. The excess urotropine was titrated. The data obtained on the primary allyl chloride contents are presented in Table 4.

Action of zinc dust. Into a liter, round-bottomed flask, fitted with a dropping funnel, a stirrer and a fractionating column, was placed 22.5 g (250% excess) of zinc dust, 150 ml of methyl alcohol and 50 ml of water. The mixture was heated to boiling and stirred, while 25 g of the addition product of chloromethyl ethyl ether and chloroprene was added dropwise. After removal of the first distillate at 70-74° (150 ml), 200 ml of water was added to the reaction flask and then a second distillate (190 ml) was collected. The first distillate was diluted with water and distilled until the moment when a clear (on dilution with water) distillate appeared. Saturation of the distillate with calcium chloride gave an oil (7.5 g). Further distillation of the aqueous layer and subsequent salting out with calcium chloride yielded a further 0.3 g of oil.

Distillation of the oil gave a low-boiling fraction with b.p. 117-118° (3.3 g), d_4^{20} 0.7879, n_D^{20} 1.4098.

Found %: C 76.40, 76.60; H 13.08, 13.04.

These data do not correspond to the formula $C_7H_{12}O$ or to the formula $C_7H_{14}O$. The spectrum of the substance is given in the figure (curve 1).

Dilution of the second distillate precipitated a heavy oil containing the original ether.

Action of alcoholic alkali. a) To a solution of 0.1 mole of the addition products of chloroprene and α-chloro- or α-bromo-ether was added a 15% alcohol solution of KOH (100 ml). When the mixture had stood for 12 hours, the precipitate of KCl or KBr was filtered off and washed with dry ether. The filtrate was diluted with water. The lower (aqueous) layer was extracted with ether. The combined ether extracts and the upper layer were washed with saturated calcium chloride solution. After being dried over $CaCl_2$, the ether was distilled at normal pressure and the residue in vacuum. The yield of glycol diether was about 80-85% (about 98% according to KCl or KBr). The properties of the compounds obtained and the analytical data are presented in Table 2.

b) 10.4 g of KOH (two-fold excess) in Cellosolve (90 ml) was added to 15 g of 1,5-dimethoxy-3-chloropentene-2. The mixture was heated on a boiling water bath for 25 minutes, diluted with water and extracted with ether.

After normal treatment of the ether layer by distillation in vacuum, we obtained a substance with the following constants.

B.p. 65-67° (10 mm), 86-94.5° (50 mm). Yield 37% (according to KCl 68%).
Found %: C 65.52; H 9.21. $C_7H_{12}O_2$. Calculated %: C 65.62; H 9.44.

The infrared spectrum of the substance is given in the figure (curve 2).

c) The action of KOH in Cellosolve on 1,5-diethoxy-3-chloropentene-2 gave a 56% yield (87% according to KCl) of a substance with the following constants: b.p. 83-86° (10 mm), 121-122° (50 mm).

Reaction with diethylamine. The addition products of chloroprene and α-halo-ethers were mixed with a two-fold excess of diethylamine with cooling. A 30% solution of NaOH was added to the mixture obtained. The upper layer was extracted with ether. The ether extracts were dried over KOH and vacuum distilled. The yield of amines was 80-85%.

The constants and analytical data are presented in Table 2.

When 16.1 g of 1-diethylamino-3-chloro-5-ethoxypentene-2 was heated with 11 g (three-fold excess) of KOH in Cellosolve for 1.5 hours, we isolated 4.9 g (85%) of KCl. Distillation in vacuum yielded a substance with b.p. 102-103° (10 mm). The yield was 59%.

Found %: C 71.90; H 11.70; N 7.59, 7.84. $C_{11}H_{21}ON$. Calculated %: C 72.13; H 11.55; N 7.64.

The infrared spectrum of the substance is given in the figure (curve 3).

SUMMARY

1. The reaction of chloroprene with α-chloro- and α-bromo- ethers $CH_2Hal - OR$ ($R = CH_3$, C_2H_5, C_3H_7 and iso-C_3H_7) was investigated.

2. It was established that the addition occurs mainly at the 1,4-position, with the halogen tending towards the fourth atom of the diene system.

3. From the addition products of halo-ethers and chloroprene we prepared halogen-containing unsaturated diethers and amino ethers. The effect of KOH in cellosolve on them was investigated.

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CONJUGATED SYSTEMS

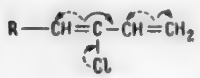
LXXXVIII.* CONDENSATION OF 3-CHLORO-1,3-PENTADIENE AND 3-CHLORO-1,3-HEXADIENE WITH PROPARGYLALDEHYDE AND PROPIOLIC ACID

E. A. Leporskaia and A. A. Petrov

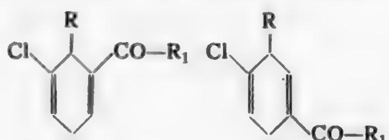
In a series of recently published papers on the direction of the diene synthesis the problem of the differing influence exerted by several dissimilar substituents on the diene system has been discussed quite inadequately [1-3]. At the same time, in the case of benzene derivatives definite arrangements of the substituents based on the magnitude of their orienting influence were established long ago [4]. We undertook to study this problem on the examples of condensing 3-chloro-1,3-pentadiene with propiolic acid and 3-chloro-1,3-hexadiene with propargylaldehyde and the same acid.

The aromatic analog of 3-chloro-1,3-pentadiene is o-chlorotoluene. In the bromination and nitration of the latter the methyl group shows a smaller orienting influence than the chlorine atom [5, 6]. In its substitution reactions the analog of 3-chloro-1,3-hexadiene is o-chloroethylbenzene, but here we were unable to find the corresponding data of the orienting influence of substituents in the literature.

Our experiments revealed that in the diene synthesis reactions involving both of the above-named halo derivatives the formation of two possible addition products (I and II) is observed in all cases, in which connection the main direction of the reaction is that which is determined by the presence of the alkyl group.



Determining the amounts of isomers with a m-alkyl group and an oxygen-containing radical (II) in the reaction products did not present any difficulties. These isomers when oxidized with dilute nitric acid give the known 4-chloroisophthalic acid in good yields. At the same time, isomer (I) suffers decomposition when oxidized.



(I) (II)

We judged the relative amounts of the two isomers by the results of the chromatographic separation of their mixture and by the amount of 4-chloroisophthalic acid formed in the oxidation of the whole mixture.

The chromatographic separation of the mixed acids obtained as products in the condensation of chloropentadiene with propiolic acid enabled us to isolate two chloromethyldihydrobenzoic acids with melting points of 122-124° and 167-169°, respectively in the ratio of approximately 3:1. The first of these acids when oxidized does not give an aromatic acid, while the second yields 4-chloroisophthalic acid. On this basis the second acid was assigned the formula of 4-chloro-3-methyl-$\Delta^{1,4}$-dihydrobenzoic acid. Only the formula of 3-chloro-2-methyl-$\Delta^{2,6}$-dihydrobenzoic acid remained for the first acid.

* Diene compounds. LXVII. Diene synthesis involving halodienes. XI.

Chromatographing of the mixed acids obtained in the condensation of the chlorohexadiene with propiolic acid gave acids with melting points 103-105° and 153-154°, also respectively in the ratio of approximately 3: 1. Oxidation of the high-melting acid gave 4-chloroisophthalic acid, on which basis the structure of 4-chloro-3-ethyl-$\Delta^{1,4}$-dihydrobenzoic acid was assigned to this isomer. Oxidation of the second isomer with nitric acid did not give an aromatic acid, and consequently only the formula of 3-chloro-2-ethyl-$\Delta^{3,6}$-dihydrobenzoic acid could be assigned to it, which was confirmed by its oxidation with potassium permanganate, where the known 3-chlorophthalic acid was obtained in very small yield. The dehydrogenation of the 3-chloro-2-ethyldihydrobenzoic acid over palladium apparently gave the previously unknown 3-chloro-2-ethylbenzoic acid.

The condensation of the chlorohexadiene with propargylaldehyde gave a chloroethyldihydrobenzaldehyde with a narrow boiling range. Treatment of the latter with methylmagnesium iodide gave a secondary alcohol, which also distilled in a narrow boiling range. However, when this aldehyde was oxidized with silver oxide we obtained a mixture of two of the acids discussed above with m.p. 103-104° and 152-154°. Only 4-chloroisophthalic acid is obtained when the mixture of aldehydes was oxidized with nitric acid. Oxidation with alkaline potassium permanganate solution gave, besides 4-chloroisophthalic acid, also a small amount of o-ethylbenzoic acid, formed by the cleavage of hydrogen chloride from the low-melting chloroethyldihydrobenzoic acid.

The presented experimental data indicate that orientation in the diene synthesis is evidently determined by somewhat different factors than is the orientation in reactions involving substitution in the benzene ring. In the case investigated by us the alkyl group exerts a greater influence on the reaction result than does the chlorine atom. At the same time, the reverse situation is observed in the case of 3-chloro-2-methyl-1,3-butadiene [3]. This is apparently due to the fact that steric factors play a greater role in the diene synthesis, in the given case the greater availability of the CH_2 = group when compared with the other end of the molecule.

EXPERIMENTAL

All of the condensations were run in toluene solution in sealed glass tubes at 110-120° for 10 hours in the presence of hydroquinone.

Condensation of 3-chloro-1,3-pentadiene with propiolic acid. From 5.7 g of the chloropentadiene and 2.5 g of propiolic acid we obtained 5.4 g (88%, based on the acid) of crystalline condensation products contaminated with polymer. The polymers were precipitated by adding water to a hot solution of the condensation products in alcohol. 4-Chloro-3-methyl-$\Delta^{1,4}$-dihydrobenzoic acid with m.p. 167-169° (0.52 g) was isolated when the obtained mixture of chloromethyldihydrobenzoic acids was recrystallized 6 times from toluene. Further recrystallizations did not change the melting point.

Found %: Cl 20.36 equiv. 170.0. $C_8H_9O_2Cl$. Calculated %: Cl 20.54. equiv. 172.6.

Oxidation of the substance with 20% nitric acid in sealed tubes at 160° for 10 hours gave an 80% yield of 4-chloroisophthalic acid with m.p. 291.5-293° (cor.) [7].

Found %: Cl 17.60 equiv. 100.0. $C_8H_5O_4Cl$. Calculated %. Cl 17.68. equiv. 100.3.

Repeated passage of the solutions obtained after removal of most of the 4-chloro-3-methyldihydrobenzoic acid through a column of aluminum oxide enabled us to isolate 3-chloro-2-methyl- $\Delta^{3,6}$-dihydrobenzoic acid with m.p. 122-124° (1.57 g).

Found %: Cl 20.11. equiv. 170.0 $C_8H_9O_2Cl$. Calculated %: Cl 20.54. equiv. 172.6.

Oxidation of the substance with 20% nitric acid gave acetic acid and traces of a substance with m.p. 264°.

Condensation of 3-chloro-1,3-hexadiene with propiolic acid. From 3.2 g of the chlorohexadiene and 1.5 g of propiolic acid we obtained 2.8 g (70%) of crystalline condensation products. In a second experiment we obtained 4.7 g (73%) of the same products from 5.8 g of the chlorohexadiene and 2.4 g of propiolic acid.

Recrystallization from toluene and chromatographic separation of the mixture led to the isolation of two acids.

1) 4-Chloro-3-ethyl-$\Delta^{1,4}$-dihydrobenzoic acid with m.p. 153-155°.

Found %: Cl 19.14. equiv. 185.0, 189.0. $C_9H_{11}O_2Cl$. Calculated %: Cl 19.00. equiv. 186.6.

Oxidation of the substance with 20% nitric acid gave 4-chloroisophthalic acid with m.p. 293.5-295.5° (cor.).

2) 3-Chloro-2-ethyl- $\Delta^{2,6}$-dihydrobenzoic acid with m.p. 103-105 (three times the amount of (1)).

Found %: C 58.01, 58.25; H 6.19, 6.23; Cl 19.24, $C_9H_{11}O_2Cl$. Calculated %: C 57.92; H 5.94, Cl 19.00.

Oxidation of the substance with 20% nitric acid gave acetic acid.

Oxidation of the original mixture of acids (1.8 g) with potassium permanganate (6.32 g) in alkaline solution (2.28 g of KOH in 40 ml of water) with heating on the water bath until the solution became colorless gave two acids–3-chlorophthalic acid with m.p. 186° [6] (about 0.01 g) and 4-chloroisophthalic acid (0.47 g), together with some lower melting acids (about 0.1 g).

Condensation of 3-chloro-1,3 hexadiene with propargylaldehyde. The mixture obtained from the condensation of 17 g of the chlorohexadiene and 10 g of propargylaldehyde was first steam-distilled and then the oil was fractionally distilled in vacuo to give 8 g (32%) of mixed chloroethyldihydrobenzaldehydes.

B.p. 130-131° (20 mm), d_4^{20} 1.1314, n_D^{20} 1.5230, MR_D 46.07; calc. 45.51.
Found %: Cl 20.57. $C_{15}H_{11}OCl$. Calculated %: Cl 20.78.

2,4-Dinitrophenylhydrazone. M.p. 202-204° (from alcohol).

Found %: N 15.87. $C_{15}H_{15}O_4N_4Cl$. Calculated %: N 15.97.

Oxidation of the condensation products with 20% nitric acid at 160° for 10 hours gave a crystalline product, from which 4-chloroisophthalic acid with m.p. 293-294° was isolated after three recrystallizations.

Oxidation of the aldehyde (6.6 g) with potassium permanganate (30.2 g) in alkaline solution (5 g KOH in 50 ml of water) gave acetic acid, an apparent polymer of the aldehyde and 3 g of mixed solid acids, about 80% of which was 4-chloro-isophthalic acid with m.p. 294°. Chromatographic separation of the acids in ethyl alcohol solution enabled us to isolate a small amount of o-ethylbenzoic acid with m.p. 66-68°.

Oxidation of the aldehyde with silver oxide in alkaline medium gave, together with the polymer, a mixture of acids, which was separated by chromatographing into two acids with m.p. 103-104° (60-70% of the mixture) and 152-154°, respectively. Both acids failed to depress the melting point when mixed with the similar substances obtained in the condensation of 3-chloro-1,3-hexadiene with propiolic acid.

Dehydrogenation of the first acid (0.17 g) by heating with palladium black gave, probably, 3-chloro-2-ethylbenzoic acid with m.p. 126-128°. The substance was not studied more closely.

Reaction of 7.5 g of the mixed chloroethyldihydrobenzaldehydes with a solution of methylmagnesium iodide in ether (20% excess) gave a mixture of two secondary alcohols–3-chloro-2-ethyl-$\Delta^{2,6}$-dihydro-α-phenylethyl and 4-chloro-3-ethyl-$\Delta^{1,4}$-dihydro-α-phenylethyl alcohols.

B.p. 129-130° (10 mm), d_4^{20} 1.1096, n_D^{20} 1.5185, MR_D 51.02; calc. 51.64.
Found %: Cl 18.74. $C_{10}H_{15}OCl$. Calculated %: Cl 18.99.

SUMMARY

1. The condensation of 3-chloro-1,3-pentadiene with propiolic acid and of 3-chloro-1,3-hexadiene with propiolic acid and with propargylaldehyde were investigated.

2. It was shown that a mixture of the two possible isomeric chloroalkyldihydrobenzoic acids or benzaldehydes is formed in all cases as a result of condensation, with the isomers having an o-alkyl group and an oxygen-containing radical present in predominant amount.

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CONJUGATED SYSTEMS

LXXXIX.* INFLUENCE OF VARIOUS FACTORS ON THE YIELD OF GERANYL CHLORIDE IN THE REACTION OF ISOPRENE WITH ITS HYDROCHLORIDES

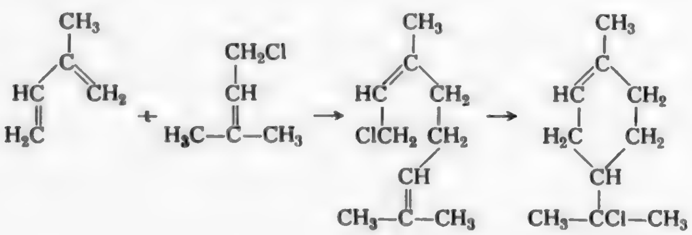
A. A. Petrov, Kh. V. Bal'ian, Iu. I. Kheruze, E. Iu. Shvarts and L. L. Cherenkova

The possibility of adding halo derivatives to diene hydrocarbons was first briefly mentioned relative to the addition of tert-butyl halides and allyl halides [1]. A more detailed study of the reaction of diene hydrocarbons with alkyl halides was made in our laboratory [2]. It was established that in the presence of zinc halides the primary, secondary and tertiary alkyl halides add to diene hydrocarbons, in which connection the reaction rate increases in the given order. Primary addition products (1 : 1 ratio) were isolated only in the case of the reaction of tert-alkyl halides with butadiene; mixtures of the higher telomers were obtained in the other cases. Some experiments were also made on the reaction of diene hydrocarbons with unsaturated halo derivatives, and successful results were obtained here also [3, 4].

The data obtained in the addition of prenyl chloride (1-chloro-3-methyl-2-butene) to isoprene with the formation of geranyl chloride deserved special attention. The fact that synthetic geranyl chloride was obtained in good yield here opened up a broad vista for both the perfume and vitamin industries. This circumstance caused a number of laboratories, including ours, to undertake a detailed study of the reaction of diene hydrocarbons with their hydrochlorides in order to determine the possibility of obtaining the optimum yields of geranyl chloride and its homologs [5, 6].

The addition of isoprene hydrochlorides to isoprene yields a complex mixture of halo derivatives with the composition $C_5H_9-(C_5H_8)_n-Cl$. In this paper we investigated only the fraction of terpene chlorides with composition $C_{10}H_{17}Cl$ ($n = 1$).

Theoretically the formation of 12 aliphatic and 2 alicyclic terpene chlorides could be expected from isoprene and its two hydrochlorides. It was unequivocally shown [6] that both geranyl chloride (conversion to citral) and terpinyl chloride (conversion to α-terpineol) are present in this mixture. Both mentioned compounds are the products of the addition of prenyl chloride to isoprene, in which connection the terpinyl chloride is formed from geranyl chloride by isomerization due to the double bond present.



* Diene compounds. LXVIII. Reaction of dienes with halo derivatives. IV.

Besides these products, the obtained mixture of terpene chlorides can also contain linalyl chloride and a substance arising from the addition of dimethylvinylchloromethane to isoprene, namely the allyl isomer of prenyl chloride. A detailed study of this mixture will be the subject of future investigations.

The results of our experiments on a study of the influence exerted by various conditions on the yield of geranyl chloride are discussed in this communication. The method developed under the direction of K. V. Leets [7] and based on the Sommelet reaction was selected by us as the principal method for determining the amount of primary chlorides of the allyl type in the mixture.

The influence of the following on the yield of geranyl chloride was investigated: 1) nature of the catalyst, 2) nature of the hydrochloride, 3) ratio of the reactants, 4) nature of the solvent, 5) temperature, and 6) degree of conversion.

We tested 15 different compounds as catalysts for this reaction. Of them only the following proved to be effective: stannic chloride, zinc chloride, ferric chloride, aluminum chloride and titanium chloride. Cuprous and cupric chlorides, mercurous and meruric chlorides, the chlorides of cobalt, lead and phosphorus, and also hydrogen chloride, zinc sulfate, benzoyl peroxide and azobisisobutyronitrile failed to show any catalytic activity.

The most effective catalyst is anhydrous stannic chloride. It causes telomerization to proceed at room temperature and lower, using concentrations of the order of a tenth of a percent on the weight of reaction mixture (Table 1, Expts. 1-19).

TABLE 1

Influence of Telomerization Reaction Conditions on Yield of Geranyl Chloride

Exp. No.	Catalyst	Hydrochloride	Degree of conversion (in %)	Density increase Δd	Solvent	Temp.	Am't of telomer (in g)	Desired fraction (in % of telomer)	Geranyl chloride: Am't in desired fraction (in %)	Geranyl chloride: yield (in %)
1			25	0.041	CH_2Cl_2	10°	24.2	48	54.5	26.0
2			29	0.048	CH_3NO_2	10	28.5	33	56.8	18.5
3			31	0.051	CH_2Cl_2	10	30.0	40	52.8	21.0
4			31	0.051	CH_2Cl_2	25	30.4	44	47.9	21.0
5			32	0.045	C_8H_{18}	10	31.5	40	46.4	18.3
6			33	0.050	CH_2Cl_2	35	32.5	42	48.8	20.6
7		1.4	34	0.064	Without solvent	30	33.0	35	39.8	19.8
8			35	0.053	CH_3NO_2	10	34.0	32	56.8	17.9
9			37	0.048	CH_2Cl_2	35	36.8	38	48.1	18.4
10	$SnCl_4$		39	0.055	CH_3NO_2	10	38.3	31	54.3	17.0
11			41	0.045	C_8H_{18}	10	39.8	35	40.7	14.4
12			43	0.058	C_8H_{18}	15	42.3	29	39.9	11.5
13			44	0.072	CH_2Cl_2	38	42.9	30	41.6	12.7
14			47	0.073	CH_2Cl_2	10	45.9	29	43.7	12.7
15			14	0.041	CH_2Cl_2	40	13.4	54	59.0	32.0
16			23	0.056	CH_2Cl_2	10	22.6	45	47.7	25.7
17		1.2	25	0.064	CH_2Cl_2	10	25.6	45	55.5	24.8
18			32	0.069	CH_2Cl_2	30	31.6	44	50.1	21.8
19			43	0.077	C_8H_{18}	10	42.0	30	42.4	12.8
20	$SnCl_4 \cdot 5H_2O$		32	0.045	CH_2Cl_2	40	31.6	44	44.3	19.6
21	$SnCl_4 \cdot 5H_2O$	1.4	44	0.075	CH_2Cl_2	40	47.5	41	33.5	13.8
22	$ZnCl_2$		33	0.037	C_8H_{18}	40	32.4	60	34.1	20.6
23	$ZnCl_2$		51	0.061	CH_2Cl_2	40	49.7	53	26.9	14.2

Stannic chloride crystal hydrate, both as a solid and in alcohol solution, is also an effective telomerization catalyst; however, its activity is lower than that of the anhydrous stannic chloride, and consequently it has to be used in larger amounts and the reaction has to be run at 35-40° (Expts. 20 and 21). That it is possible to use this catalyst is indicated by the fact that small amounts of moisture do not interfere with the reaction.

A disadvantage of stannic chloride is the fact that it favors the formation of substantial amounts of higher telomerization products. In the presence of this catalyst it is necessary to stop the process when only 20-30% of the isoprene has been consumed in order to obtain geranyl chloride in a yield of about 25% on consumed isoprene.

Zinc chloride is also an active telomerization catalyst. Its use in alcohol solution at 40° makes it possible to substantially improve the yield of terpene chlorides at the expense of reducing the yield of higher telomers; however, the yield of geranyl chloride based on isoprene remains the same as in the case of using stannic chloride (Expts. 22 and 23). The yield of terpene chlorides increases as the amount of this catalyst is increased.

Ferric chloride is an active telomerization catalyst (anhydrous, as solid crystal hydrate, and in alcohol solution). The yield of terpene chlorides in the presence of this catalyst is lower than in the presence of the first two discussed.

Aluminum chloride was used in ether solution. The reaction went only on heating. Strong tarring of the products occurred during distillation.

The reaction with titanium chloride goes slowly. It is necessary to use larger amounts of this catalyst.

The presented data caused us to choose two catalysts—stannic chloride (either anhydrous or as the crystal hydrate) and zinc chloride – for further studies.

The two isomeric isoprene hydrochlorides react at a different rate with isoprene in the telomerization reaction. Prenyl chloride reacts several times faster than does dimethylvinylchloromethane. However, for the same degree of conversion, the yield of geranyl chloride is not affected by this (Expts. 11, 19; 3, 4, 18; 1, 16, 17). Since the telomerization reaction in the presence of metal chlorides undoubtedly has an ionic character, and since the two isomeric isoprene hydrochlorides have the same common ion, then the addition products should have approximately the same composition independent of the structure of the starting halo derivative, which is what was actually observed. The ratio of isoprene to its hydrochlorides was varied from 1 : 0.5 to 1 : 2. The yield of terpene chlorides increased somewhat as the amount of starting chloride was increased, but this increase was less than the increased consumption of hydrochloride.

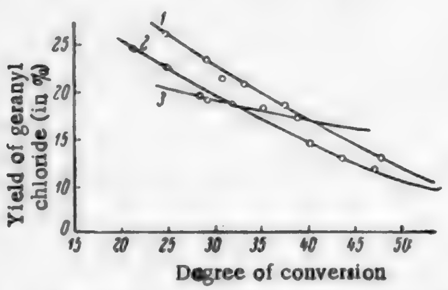


Fig. 1. Influence of the nature of the solvent and the degree of telomerization on the yield of geranyl chloride. 1) methylene chloride, 2) n-octane, 3) nitromethane

Compounds with sharply different polar properties were tested as solvents: n-octane, methylene chloride and nitromethane. For the same small degree of conversion the nature of the solvent was practically without effect on the yield of geranyl chloride. The best results were always obtained in methylene chloride. In nitromethane a less sharp reduction in the yield of geranyl chloride was observed as the degree of telomerization was increased (see Fig. 1). Approximately the same yields of geranyl chloride were also obtained when operating without a solvent, but it is difficult to regulate the reaction rate in the absence of a solvent (Expts. 12 and 13; 2, 4, and 5; 7, 8, and 9).

Temperature influences only the reaction rate (Expts. 3, 4 and 6; 13 and 14).

The single factor that strongly influences the yield of primary terpene chlorides is the degree of conversion. When the degree of conversion is 25% the yield of geranyl chloride is about 25%, when the degree of conversion is 30% the yield drops to 20% and, finally, when the degree of conversion is 45% the total yield of geranyl chloride is only 12-13% (Expts. 1, 3, and 4; 6, 9, and 13; 11 and 12).

The presented data permit the conclusion that to obtain a geranyl chloride suitable for conversion to citral it is possible to use a misture of the two isomeric isoprene hydrochlorides. If together with geranyl chloride it is desired to use the higher telomers, for example farnesyl chloride, then stannic chloride is the best

catalyst; it proves feasible to use only the cyclic terpene chlorides, then zinc chloride possesses certain advantages. In all cases the degree of conversion should be low. As regards the other conditions (temperature, solvents, reactant ratios), then they exert a smaller influence on the yield of geranyl chloride.

Since regulating the degree of conversion determines the success of synthesizing geranyl chloride from isoprene, we undertook a detailed study of methods to arrest the telomerization reaction at a given stage. Earlier it had been proposed to terminate the telomerization reaction by adding water or aqueous salt solutions to the reaction mixture [3, 5]. This method made subsequent workup extremely difficult and caused gross contamination of the end products by substances formed as a result of their hydrolysis. Much better results were achieved when solid, liquid and gaseous inorganic and organic amino compounds were used as agents to arrest the telomerization reaction [8]. Compounds of the indicated type react with the catalyst to yield complexes that are both devoid of catalytic activity and insoluble in the mixture of telomers. The addition products of amines to stannic chloride belong to the class of tetraacidoamino compounds with the tin having a coordination number of 6. Zinc chloride yields similar compounds with a coordination number of 4 [9]. As "quenching agents" we tested ammonia (both as a gas and on activated carbon), ammonium carbonate, diethylamine, triethylamine, tribenzylamine, aniline, methylaniline, pyridine, urea, thiourea, melamine, etc. All of the enumerated compounds terminate the telomerization reaction, but at a different rate. Under laboratory conditions we found liquid "quenching agents" to be the most satisfactory. The yield of geranyl chloride does not depend on the nature of the "quenching agent".

In order to characterize in more detail the products obtained in the telomerization of isoprene with its hydrochlorides we fractionally distilled the products obtained in three of the experiments. From these experiments it can be seen that the major portion of the terpene chlorides distills in a 5-7° range. We took the main fractions of the terpene chloride specimens and determined both their infrared spectra and the amount of geranyl chloride contained in them. In the experiments using stannic chloride the main terpene chloride fraction contained about 50% geranyl chloride, while in the experiments with zinc chloride the geranyl chloride content was about 25%. In all cases the amount of dienic halo derivatives proved to be greater than the amount of geranyl chloride. Consequently, these fractions contain an isomeric chloride, apparently linalyl chloride.

The infrared spectra of the main fractions from all three experiments proved to be similar. In order to determine the possibility of using these spectra for the qualitative and quantitative determination of the amounts of geranyl, linalyl and terpinyl chlorides in the telomerization products we attempted to prepare these compounds in the pure state from the corresponding alcohols and investigate their infrared spectra. Pure terpinyl chloride was obtained from crystalline synthetic terpineol. We were able to obtain the geranyl chloride only 86% pure. Linalyl chloride could not be isolated in a concentration greater than 50%. A comparison of the spectra of geranyl and terpinyl chlorides led to the conclusion that an intense frequency at 835 cm^{-1} is characteristic for the first compound, and one at about 790 cm^{-1} (doublet) for the second. It should also be mentioned that terpinyl chloride shows much stronger adsorption than geranyl chloride at 1150 cm^{-1}. In the spectrum of geraniol the 835 cm^{-1} frequency has a weak intensity. On the contrary, α-terpineol, the same as terpinyl chloride, shows strong adsorption at 790 cm^{-1}. The spectrum of linalool has intense frequencies at 916 and 988 cm^{-1}, characteristic for the vinyl group. Apparently, linalyl chloride should also absorb in this region. Only the higher frequency can be used to determine linalyl chloride, since the frequency in the vincinity of 916 cm^{-1} is also found in the spectrum of terpinyl chloride.

Based on the presented data it becomes possible to make some conclusions relative to the composition of the terpene chlorides obtained as products in the telomerization of isoprene with its hydrochlorides. As can be seen from Fig. 2, all three investigated mixtures contain geranyl chloride (frequency 835 cm^{-1}), terpinyl chloride (frequency 790 cm^{-1}) and linalyl chloride (frequency 988 cm^{-1}). Apparently, these mixtures also contain some other chloride, showing intense absorption around 910 cm^{-1}. Based on the ratio of the intensities of the characteristic frequencies it can be concluded that the above three terpene chlorides are formed in close amounts from both isoprene hydrochlorides. The amount of terpinyl chloride in the mixture increases sharply when zinc chloride is used as the catalyst. This conclusion is in agreement with the chemical data.

The infrared spectrum in the regionof 6.060 cm^{-1} can also be used to analyze mixtures of terpene chlorides. As is known, compounds containing the vinyl group have a characteristic frequency ($^{\nu}$Ch overtone) in this region. Terpineol, geraniol and their chlorohydrins do not absorb in this region. Linalool has an intense overtone at 6.060 cm^{-1}.

The mixtures of terpene chlorides obtained by telomerization absorbed at 6.060 cm^{-1}, and therefore undoubtedly contained the product of the addition of prenyl chloride to isoprene in the 1,2 position, i.e. linalyl

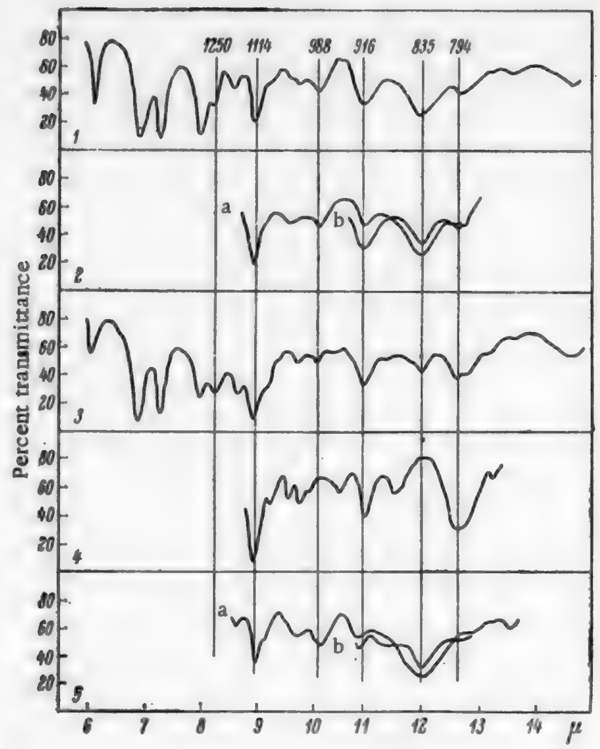


Fig. 2. Infrared spectra of the products obtained in the telomerization of isoprene with its hydrochlorides. 1) prenyl chloride and isoprene in the presence of $SnCl_4$, 2) dimethylvinylchloromethane and isoprene in the presence of $SnCl_4$: a) fraction 79-81° (5 mm), b) fraction 77-79° (5 mm); 3) prenyl chloride and isoprene in the presence of $ZnCl_2$, 4) terpinyl chloride, 5) geranyl chloride; a) geranyl chloride content 86%, b) geranyl chloride content 65%.

chloride. Judging by the intensity of absorption, the amount of the latter in the terpene chlorides obtained by telomerization in the presence of stannic chloride was considerably higher than in the chlorides obtained by telomerization in the presence of zinc chloride.

EXPERIMENTAL

Hydrochlorination of isoprene. The synthesis of the isoprene hydrochlorides was run in an apparatus fitted with a disc sparger made of Shott glass No. 1. It was observed that both reducing the temperature and adding either ether or small amounts of water to the mixture hasten the process considerably. The ratio of the isomeric hydrochlorides in the final product depends on the conditions used. Raising the temperature, the presence of moisture, and mainly increasing the degree of hydrochlorination, favor the formation of the primary chloride (prenyl chloride). Depending on the indicated factors, this ratio in different experiments varied from 2 : 1 to 1 : 4 (tertiary: primary hydrochlorides).

After the desired weight increase had been obtained, the mixture of hydrochlorides was vacuum-distilled throug a Widmer column (80 cm). Distillation at atmospheric pressure causes a part of the tertiary hydrochloride to isomerize to the primary. The yield of isomeric hydrochlorides was about 70-80%. The distillation flask always contained a large amount of residue, which was not investigated more closely.

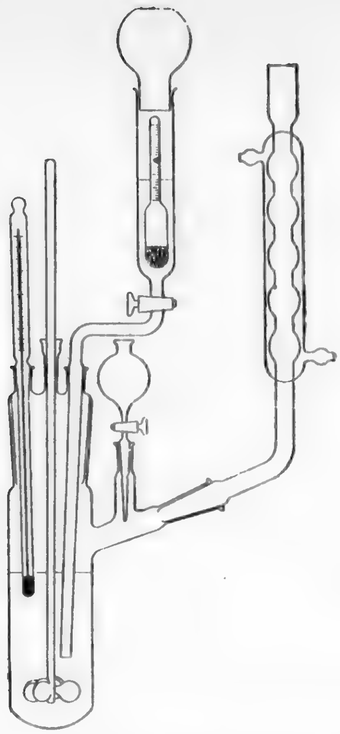


Fig. 3. Apparatus for running the telomerization reaction.

Various constants are given in the literature for the isoprene hydrochlorides. We operated with the following specimens.

3-Chloro-3-methyl-1-butene. B.p. 29-30° (120 mm), d_4^{20} 0.8845, n_D^{20} 1.4190. The amount of primary chloride, by the Sommelet-Leets method, was 10%.

1-Chloro-3-methyl-2-butene. B.p. 39-40° (50 mm), d_4^{20} 0.9290, n_D^{20} 1.4500. Amount of primary chloride 97%.

These constants are in close agreement with those given by Laforgue [10].

Telomerization. The telomerizations were run in the apparatus shown in Fig. 3, which made it possible to control the degree of conversion by the change in the specific gravity of the mixture. For this the liquid was transferred from time to time using a bulb to a vessel containing a hydrometer, and after taking a rapid reading was returned to the reaction vessel. In all of the experiments given in Table 1 the following mixture was taken for reaction: isoprene – 39 g, hydrochloride – 60 g, solvent – 20–25% by volume. The catalyst was added through the funnel. In the experiments with stannic chloride a 5% solution in methylene chloride was used. From 1.5-2 ml of this solution was added to the reaction mixture. In the experiments with zinc chloride a 20% solution in methyl alcohol was used. From 3-5 ml of this solution was added. In the experiments using solid catalysts the latter were added in an amount of 0.1 - 0.2 g through the opening for the dropping funnel. External cooling was used to regulate the reaction rate. With an efficient stirrer this was not difficult.

TABLE 2

Results of the Telomerization of Prenyl Chloride With Isoprene in the Presence of $SnCl_4$ (Isoprene 117 g, prenyl chloride 180 g, degree of telomerization 36%, catalyst $SnCl_4$)

Fraction No.	Boiling point (5 mm)	Weight (in g)	d_4^{20}	n_D^{20}	% Cl	Amount of geranyl chloride (in %)	Amount of dienic chlorides (in %)
1	To 76°	1.0	—	1.4735	—	—	—
2	76— 79	5.2	0.9348	1.4745	19.65	40.5	—
3	79— 82	21.8	0.9357	1.4775	20.10	52.0	73.4
4	82— 90	2.0	0.9545	1.4798	19.60	—	—
5	90—105	3.5	0.9728	1.4800	18.80	—	—
6	105—140	11.0	—	—	10.20	—	—
7	Residue	44.5	—	—	—	—	—

When the desired increase in the density had been reached (selected experimentally, the density was varied in a range of 0.03) the "quenching agent", in most cases pyridine, was added to the mixture through a dropping funnel. The solid quenching agents work much slower and should be used in larger amounts; however, in a continuous process they are more convenient than the liquid quenching agents.

When the reaction had been terminated and the catalyst separated as the complex, the mixture was fractionally distilled in vacuo. The solvent and reactants were distilled at 50-100 mm. Then the pressure was

reduced to 2-3 mm and the portion of the product boiling below 140° was rapidly distilled. The distilled product was refractionated. The terpene chlorides were collected in the range 60-90°. The amount of primary chlorides (geranyl chloride) in this fraction was determined by the Sommelet–Leets method [7]. A total of more than 100 experiments was made; the data of some are given in Table 1. Their reproducibility was satisfactory.

TABLE 3

Results of the Telomerization of Dimethylvinylchloromethane With Isoprene in the Presence of $SnCl_4$ (Isoprene 117 g, dimethylvinylchloromethane 178 g, catalyst $SnCl_4$, degree of telomerization 37%)

Fraction No.	Boiling point (5 mm)	Weight (in g)	d_4^{20}	n_D^{20}	% Cl	Amount of geranyl chloride (in %)	Amount of dienic chlorides (in %)
1	To 77°	2.8	—	1.4712	17.5	33.0	—
2	77—79	14.5	0.9320	1.4760	20.55 *	44.6	62
3	79—81	10.5	0.9360	1.4795	21.60	62.5	63
4	81—85	3.4	0.9443	1.4794	19.35	—	—
5	85—90	1.4	—	1.4815	—	—	—
6	90—105	2.8	0.9798	1.4803	20.5 **	— ***	—
7	105—140	4.5	—	—	11.4	—	—
8	Residue	56.5	—	—	—	—	—

The data of the larger scale experiments are given in Table 2-4. The amount of dienic chlorides in some of the experiments was established by the Kaufman method.

α-Terpinyl chloride, with b.p. 87-88° (8 mm), d_4^{20} 0.9742, n_D^{20} 1.4840, and chlorine content 20.1%, was obtained from synthetic inactive α-terpineol, with m.p. 33°, b.p. 108-109° (20 mm), d_4^{20} 0.9347, n_D^{20} 1.4818, and melting point of nitrosochloride 112° [11].

TABLE 4

Results of the Telomerization of Prenyl Chloride With Isoprene in the Presence of $ZnCl_2$ (Isoprene 78 g, prenyl chloride 120 g, catalyst $ZnCl_2$, degree of conversion 43%)

Fraction No.	Boiling point (5 mm)	Weight (in g)	d_4^{20}	n_D^{20}	% Cl	Amount of geranyl chloride (in %)	Amount of dienic chlorides (in %)
1	To 65°	1.0	—	—	—	—	—
2	65—75	3.8	0.9390	1.4742	14.9	—	—
3	75—79	7.8	0.9411	1.4745	17.6	21.5	—
4	79—82	18.0	0.9479	1.4756	19.5	26.5	35.6
5	82—90	1.0	—	1.4740	—	—	—
6	90—105	7.8	0.9447	1.4742	19.1	—	—
7	105—140	10.0	—	1.4872	12.0	—	—
8	Residue	20.1	—	—	—	—	—

* Total chlorine by the Carius method, 20.1%.

** Total chlorine by the Carius method, 26.5%.

*** Amount of primary chlorides 37%.

Geranyl chloride, with b.p. 93-95° (9 mm), d_4^{20} 0.9261, n_D^{20} 1.4795, and a geranyl chloride content 86%, was obtained by reacting phosphorus trichloride with linalool [b.p. 82° (10 mm), d_4^{20} 0.8655, n_D^{20} 1.4628, α_D+ + 14.6°]. In a second experiment using the same reactants we obtained a product with b.p. 75-80° (5 mm), d_4^{18} 0.9289 and n_D^{20} 1.4775, with a geranyl chloride content of 65%.*

SUMMARY

1. The telomerization of isoprene with its hydrochlorides in the presence of various catalysts was studied. It was shown that the best catalysts are stannic chloride and zinc chloride.

2. It was established that the character of the telomerization depends on the nature of the catalyst: stannic chloride favors the formation, together with geranyl chloride, of higher telomers, while zinc chloride favors the formation of terpinyl chloride.

3. It was shown that when stannic chloride and zinc chloride are used as catalysts the yield of geranyl chloride depends primarily on the degree of conversion, and with the same degree of conversion is nearly independent of the nature of the catalyst, nature of the halo derivative, temperature, or the reactant ratio, and is slightly dependent on the nature of the solvent.

4. It was shown that the composition of the mixed terpene chlorides formed in telomerization can be determined from the intensities of the frequencies of the infrared spectrum in the region of 1.6 and 10-12 μ.

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**See C.B. Translation.

ACETYLENE DERIVATIVES

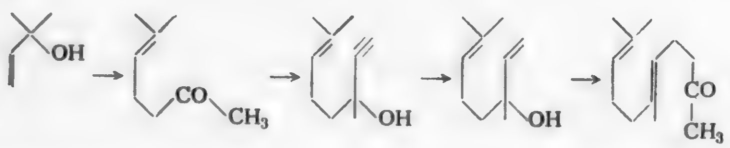
193. TOTAL SYNTHESIS OF ISOPRENOID ALCOHOLS (LINALOOL, GERANIOL, NEROL, NEROLIDOL, FARNESOL, GERANYLLINALOOL, GERANYLGERANIOL AND PHYTOL)

I. N. Nazarov,* B. P. Gusev and V. I. Gunar

Some 7 years ago we developed in our laboratory a simple method for the synthesis of acetylenic alcohols based on the condensation of aldehydes and ketones with acetylene under the influence of powdered potassium hydroxide and employing a slight pressure (5-10 atm) [1]. As is known, acetylenic alcohols in the presence of Pd-catalyst show quite selective hydrogenation and after the absorption of 1 mole of hydrogen are converted to the corresponding vinyl alcohols in nearly quantitative yield [2].

Earlier it had been shown [3] that tertiary vinyl alcohols when reacted with hydrogen halides are converted even in the cold almost completely into primary halo derivatives of allylic type, which are saponified with rearrangement to the original tertiary vinyl alcohols, and when reacted with salts of acids, followed by saponification, give primary alcohols of allylic type.

In view of the fact that dimethylvinylcarbinol has become a readily available technical product at the present time, we decided to make a detailed study of methods for the total synthesis of natural isoprenoid alcohols based on it (and also based on isoprene), employing for this purpose the multiple repetition of the following cycle of reactions:

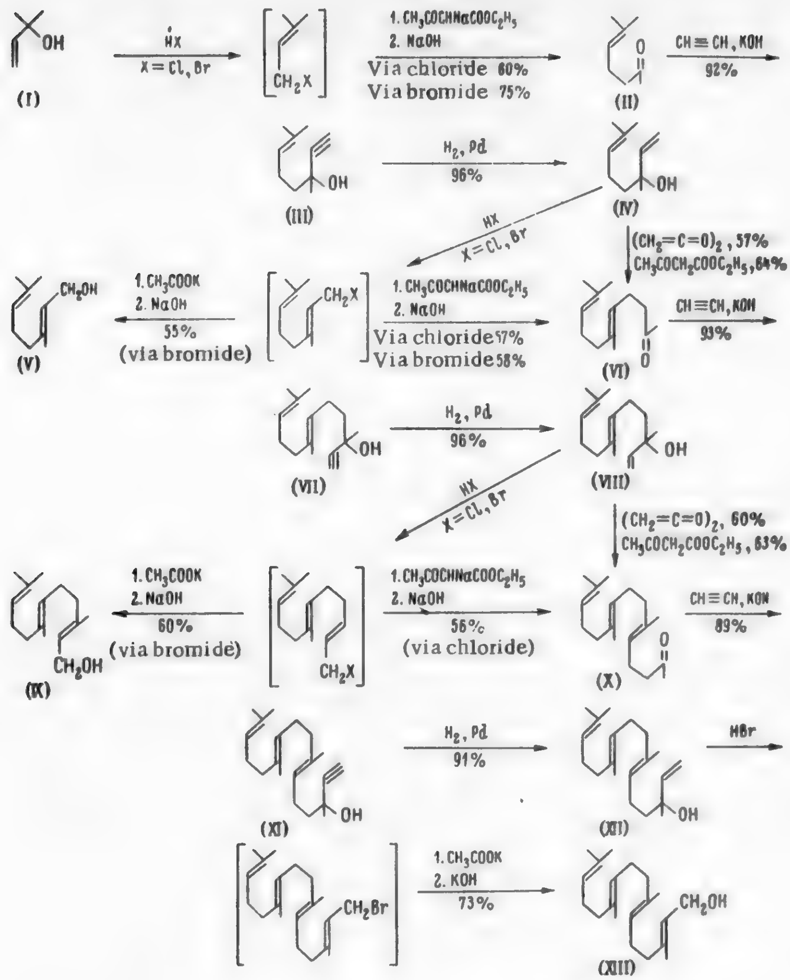


Consequently, with such a scheme the isoprenoid chain is built by a successive coupling of the reactions of ethynylation, selective hydrogenation, isomerization and acetonylation, in which connection the last two reactions are usually run in one step without isolating the intermediate products. We made a detailed study of the entire path of this synthesis up to the isoprenoid alcohols C_{20} (geranylgeraniol and phytol), the results of which are represented by the schemes shown on the next page.

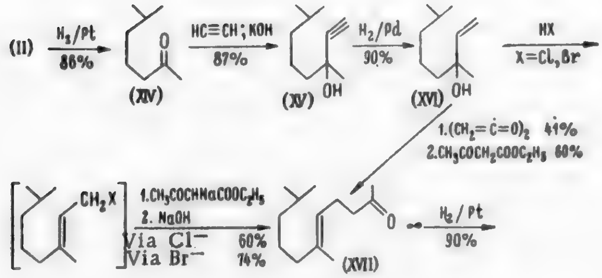
In all cases the condensation of ketones (II, VI, X, XIV, XVIII, XXII) with acetylene was run by the earlier developed method [1] in the presence of powdered potassium hydroxide under an acetylene pressure of 5-10 atm, and here the tertiary acetylenic alcohols (III, VII, XI, XV, XIX, XXIII) were obtained in 87-93% yield. In the presence of palladium on calcium carbonate the obtained acetylenic alcohols smoothly underwent selective hydrogenation (1 mole of hydrogen) to yield the corresponding tertiary vinyl alcohols (IV, VIII, XII, XVI, XX, XXIV) in 90-96% yield. The tertiary vinyl alcohols were then converted to the unsaturated ketones (II), (VI), (X), (XVII) and (XXI) (acetonylation reaction) by three different methods, all of which had recently been studied in detail in our laboratory [19].

* Deceased.

Synthesis of Geraniol (V), Farnesol (IX) and Geranylgeraniol (XIII)



Synthesis of Phytol (XXV)



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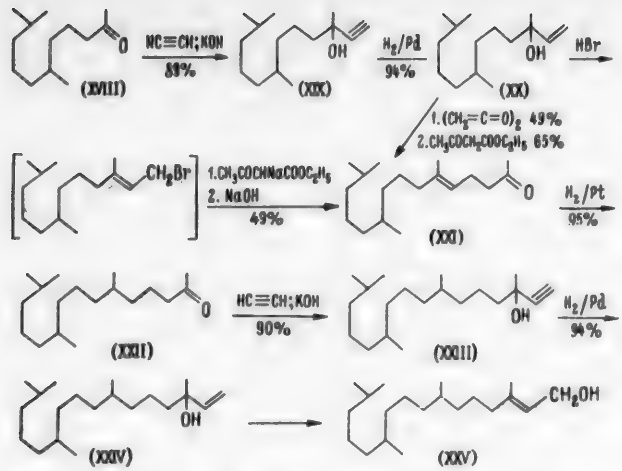


Method A. Reaction of vinyl alcohols with either gaseous hydrogen chloride or hydrogen bromide (usually in isooctane solution), with subsequent condensation of the allylic halo derivative with sodioacetoacetic ester, and saponification.

$$>\overset{\displaystyle OH}{\overset{|}{C}}-CH=CH_2 \xrightarrow{HX} >C=CHCH_2X \longrightarrow >C=CHCH_2CH_2COCH_3$$

It is expedient to run these reactions in one step without isolating the intermediate products, and here the unsaturated ketones (analogs of allylacetone) are obtained in 50-75% yield based on taken vinyl alcohol. Usually somewhat higher yields are obtained with the bromides than when the chlorides are used.

Method B. Direct reaction of tertiary vinyl alcohols with acetoacetic ester at 140-200°, with simultaneous cleavage of alcohol and carbon dioxide [4].

$$>\overset{\displaystyle OH}{\overset{|}{C}}-CH=CH_2 \longrightarrow \left[>\overset{\displaystyle OCOCH_2COCH_3}{\overset{|}{C}}-CH=CH_2\right] \longrightarrow >C=CH-CH_2CH_2COCH_3$$

With this method the unsaturated ketones (II), (VI), (X), (XVII) and (XXI) are obtained in 60-65% yield (based on vinyl alcohol), and this method is most suitable for operating on a larger scale.

Method C. Reaction of tertiary vinyl alcohols with diketene (in the presence of pyridine or triethylamine), followed by pyrolysis of the acetoacetic ester, obtained here in about 90% yield, at 170-200° [5].

$$>\overset{\displaystyle OH}{\overset{|}{C}}-CH=CH_2 \longrightarrow >\overset{\displaystyle OCOCH_2COCH_3}{\overset{|}{C}}-CH=CH_2 \longrightarrow >C=CHCH_2CH_2COCH_3$$

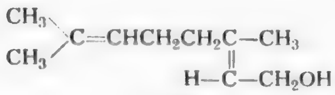
The yield of unsaturated ketones by this method is 40-60% (based on vinyl alcohol), and the reaction can be run in one step without isolating the pure acetoacetic ester.

We also made a detailed study of various methods for the conversion of the tertiary vinyl alcohols (IV), (VIII), (XII) and (XXIV) to the corresponding terpene primary alcohols–geraniol (V), farnesol (IX), geranylgeraniol (XIII) and phytol (XXV). Direct isomerization of the tertiary vinyl alcohols using sulfuric acid [6] proved to be completely unsuitable in the present case. Reaction of the tertiary vinyl alcohols with acetic anhydride in the presence of acids, followed by saponification, also did not give very satisfactory results. The best results were obtained by reacting the tertiary vinyl alcohols with either gaseous hydrogen bromide on hydrogen chloride (in isooctane solution), followed by reaction of the allylic bromides with potassium acetate in

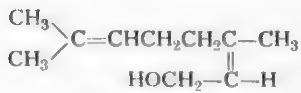
dimethylformamide solution, and then saponification of the formed acetates with 10% caustic.

All of these reactions were run in one step without isolating the intermediate products, which made it possible to increase the yields of primary terpene alcohols substantially and simplify their method of preparation. The reaction of the allylic halo derivatives with potassium acetate is best run in dimethylformamide solution. Satisfactory results are also obtained in alcohol solutions (methanol, ethanol); however, here the corresponding ethers (methyl, ethyl) of the primary terpene alcohols are formed as by-products. Other solvents (dioxane, acetone) give poorer results, apparently due to the poor solubility of potassium acetate in them. The use in this reaction of sodium acetate, or of the sodium and potassium salts of other acids (formic, butyric, benzoic), also does not give good results.

With the above-described method linalool (IV) is isomerized to a mixture of geraniol (V) and nerol (Va) in the ratio 5 : 3, in a total yield of 55-60%. These geometric isomers can be easily separated by chromatographing on aluminum oxide; here the nerol is completely eluted with petroleum ether, and the geraniol with methanol.



(V)



(Va)

Consequently, we were the first to accomplish the total synthesis of nerol, extremely important in perfumery and a very difficultly available terpene alcohol found in small amounts together with geraniol in certain valuable essential oils (rose oil, bergamot oil, tuberose oil, etc.).

With the same method nerolidol (VIII) is converted in 60% yield to farnesol, formed only as the isomer corresponding to the natural compound. As is known, it is very difficult to obtain farnesol from natural sources. It is the odor principle found in linden blossoms, and in the seeds of the musk and some other plants, containing it in small concentrations. Farnesol is of interest not only for perfumery, but also for the further synthesis of a number of natural and biologically active compounds.

The conversion of geranyllinalool (XII) to geranylgeraniol (XIII) goes even more smoothly; here, the same as in the case of farnesol, only one isomer is formed in 73% yield. The same method was also used to synthesize isophytol (XXIV), as shown in the scheme given previously.

Phytol is one of the more important natural alcohols. As is known, it is found in chlorophyll, which at the present time serves as the only natural source for obtaining it. The practical importance of phytol, and also of geranylgeraniol and the alcohols (XXIV) and (XII) isomeric with it, is associated primarily with the synthesis of vitamins K and E (tocopherol) and other biologically important compounds.

The availability of the starting products, simplicity of the operations, and the high yields at all stages, make the above described synthesis entirely suitable for the commercial preparation of isoprenoid alcohols (linalool, geraniol, nerol, nerolidol, farnesol, geranyllinalool, geranylgeraniol and phytol), representing great interest for perfumery and the synthesis of some important natural compounds (vitamins A, E and K, carotenoids, terpenes, etc.).

The above scheme for the synthesis of isoprenoid alcohols also repeatedly attracted the attention of earlier investigators [7-11]. However, up to now this scheme remained quite undeveloped and was completely unsuitable for the large-scale production of isoprenoid alcohols, since all three repeating steps of this synthesis (ethynylation, acetonylation and isomerization of tertiary vinyl alcohols to primary terpene alcohols) were in their methods either unsuitable for large-scale operation or gave low yields.

In particular, the major difficulties were encountered in the condensation of acetylene with unsaturated ketones (of the allylacetone type), which was usually run in liquid ammonia solution, gave quite low yields of

the corresponding acetylenic alcohols, was difficult to run, and was unsuitable for operating with large quantities of material. The main drawbacks encountered in the isomerization of tertiary vinyl alcohols to primary terpene alcohols were the low yields, which usually did not exceed 20-30%. A basic improvement in all of the schemes for the synthesis of isoprenoid alcohols was also achieved by combining the above mentioned isomerization of tertiary vinyl alcohols with acetonylation, running the two as one operation with the yield of unsaturated ketones–analogs of allylacetone–being equal to 60-75%, based on taken tertiary vinyl alcohol.

EXPERIMENTAL

Preparation of methylheptenone (II). a) A stream of 193 g (2.4% excess)of hydrogen bromide was passed in 3 hours into 200 g of dimethylvinylcarbinol (I) with ice-water cooling. After holding at room temperature for 90 minutes the aqueous layer (40 ml) was separated, the bromide washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 323 g of crude bromide, which without further purification was added in an hour at 0-5° to a solution of sodioacetoacetic ester, prepared from 55 g of sodium metal and 380 g of acetoacetic ester in 650 ml of anhydrous alcohol. The reaction mixture was stirred for 3 hours at room temperature and for 4 hours at 60°, after which the precipitate of sodium bromide (213 g) was filtered, the alcohol distilled under slight vacuum, and the residue treated with 1 liter of 10% sodium hydroxide solution. The mixture was stirred vigorously for 2 hours at room temperature and for 3 hours at 60-65°, cooled, acidified with concentrated hydrochloric acid (to Congo), the methylheptenone extracted with ether, the ether extract washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate. After removal of the ether by distillation the residue was first vacuum-distilled and then through a column with an efficiency of 25 theoretical plates. We obtained 219 g (75%, based on dimethylvinylcarbinol) of methylheptenone.

B.p. 75.5-76° (25 mm), n_D^{20} 1.4404, d_4^{20} 0.8615, MR 38.89; calculated 38.69.

The semicarbazone had m.p. 135.5-136° (from 80% ethanol)[12].

b) A stream of 39.5 g (8% excess) of hydrogen chloride was passed in 4 hours into 86 g of dimethylvinylcarbinol with ice-water cooling. After holding at room temperature for 2 hours the aqueous layer (20 ml) was separated, the chloride washed with saturated bicarbonate solution, and then dried over magnesium sulfate. The chloride without further purification was used in the reactions with sodioacetoacetic ester.

The above-described chloride was added in 90 minutes to a solution of sodioacetoacetic ester prepared from 34 g of sodium metal and 190 ml of acetoacetic ester in 300 ml of methanol. The temperature of the reaction mass was 30-40°. The mixture was stirred at this temperature for another 2 hours, after which the methanol was distilled off, and the residue was treated with 600 ml of 10% sodium hydroxide solution. After stirring at 60-70° for 3 hours the reaction mixture was cooled, acidified with concentrated hydrochloric acid (to Congo), the methylheptenone layer was separated, the aqueous layer was extracted 4 times with ether, the combined ether solution was washed with saturated sodium bicarbonate solution, then with water, and finally dried over magnesium sulfate, After removal of the ether by distillation the residue was vacuum-distilled. We obtained 76.3 g (60%) of methylheptenone with b.p. 54-56° (9 mm); n_D^{21} 1.4397.

The semicarbazone had m.p. 135-136°.

The preparation of methylheptenone by methods B and C had been described by us earlier [19].

Preparation of dehydrolinalool (III). Into a 6-liter steel reactor [1] was charged 3.5 liters of absolute ether, 360 g of powdered potassium hydroxide and 20 ml of ethanol. After blowing with nitrogen the reaction mass was saturated with acetylene to a pressure of 6 atm, and then 680 g of methylheptenone was added from a steel dropping funnel under pressure in 1.5 hours at 2-4°. The reaction mass was stirred under an acetylene pressure of 6-7 atm for 2 hours at 4-5° and for 2 hours at room temperature. Then the excess acetylene was removed and 720 ml of water was added, the mixture stirred vigorously for 15 minutes, the ether layer separated, the aqueous layer extracted with ether, and the combined ether solution neutralized with carbon dioxide and dried over magnesium sulfate. The ether was removed by distillation and the residue was vacuum-distilled. We obtained 750 g (92%) of dehydrolinalool.

B.p. 82-83° (10 mm), n_D^{20} 1.4632, d_4^{20} 0.8788 [13], MR 47.44; calculated 47.63.

Preparation of linalool (IV). Into a 3-liter steel reactor, fitted with stirrer and water jacket for cooling, was charged 740 g of dehydrolinalool and 1.2 g of palladium catalyst, deposited on calcium carbonate. The hydrogenation was run at 12-15° (with cooling) and a hydrogen pressure of 2-3 atm. The amount of hydrogen absorbed in 2.5 hours was 110 liters, after which the test for acetylenic hydrogen showed negative. (The sensitivity of the acetylenic test using an ammoniacal solution of silver nitrate in alcohol is 0.3-0.5%). We obtained 723 g (96%) of linalool.

B.p. 80-82° (10 mm) [13], n_D^{20} 1.4622, d_4^{20} 0.8664, MR 48.96; calculated 48.97.

Found %: C 77.59, 77.64; H 11.87, 11.86. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.80.

By means of special experiments it was established that the degree of selectivity shown by dimethylethynylcarbinol when hydrogenated with Pd-catalyst on calcium carbonate is not less than 99.5%. Other acetylenic alcohols, containing unsubstituted acetylenic hydrogen, also hydrogenate in a similar manner. Platinum and nickel catalysts lack the ability of promoting the selective hydrogenation of acetylenic alcohols and cannot be used in these reactions to obtain pure vinyl alcohols. All of the other acetylenic alcohols were hydrogenated in the same manner as described above; large quantities (over 200 g) were hydrogenated in a steel reactor under pressure, while small amounts (under 200 g) were hydrogenated in a glass bottle at atmospheric pressure. The palladium catalyst, deposited on calcium carbonate, was prepared in conventional manner [14], and contained about 5% palladium.

Isomerization of linalool to geraniol (V) and nerol (Va). A stream of 85 g (5% excess) of hydrogen bromide was passed in 1 hour into 154 g of linalool at 5°. After holding at room temperature for 2 hours the aqueous layer (18 ml) was separated, the bromide washed quickly with cold saturated bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 184 g of crude bromide, which was added in 15 minutes at room temperature to a solution of 98 g of potassium acetate in 700 ml of dimethylformamide (the potassium acetate dissolved only partially). Then the mixture was stirred for 2 hours at room temperature and for 2 hours at 45-50°. The precipitate of potassium bromide (112 g) was filtered, while the dimethylformamide was vacuum-distilled at 20 mm. The residue was treated with 800 ml of 10% sodium hydroxide solution and the mixture stirred for 4 hours at 70°. The product was extracted with ether and dried over magnesium sulfate. The ether was removed by distillation and the residue was vacuum-distilled. We obtained 92 g of mixed geraniol and nerol with b.p. 103-110° (9 mm), n_D^{20} 1.4754, which was easily separated by chromatographing through a column containing aluminum oxide (activity II, diameter of column 32 mm, height 700 mm). Elution with 1 liter of petroleum ether enabled us to isolate 31.2 g (20%, based on linalool) of nerol.

B.p. 103-105° (9 mm), n_D^{20} 1.4744, d_4^{20} 0.8762, MR 49.50; calculated 48.96.

Calculated %: C 77.93, 77.77; H 11.80, 11.71. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.68

The diphenylurethan had m.p. 50.5-51° [15].

Elution with 500 ml of methanol gave us 53.8 g (35%, based on linalool) of geraniol.

B.p. 109-100° (9 mm), n_D^{20} 1.4760, d_4^{20} 0.8806, MR 49.39; calculated 48.96.

Found %: C 77.60, 77.52; H 11.76, 11.72. $C_{10}H_{18}O$. Calculated %: C 77.87; H 11.68.

The diphenylurethan had m.p. 81-81.5° [16].

Preparation of geranylacetone (VI). Method A. a) A stream of 165 g (1.8% excess) of hydrogen bromide was passed in 2 hours into 308 g of linalool with ice-water cooling. After holding at room temperature for 2 hours the aqueous layer (35 ml) was separated, the bromide washed quickly with saturated bicarbonate solution, then with water, and finally dried over magnesium sulfate. We obtained 418 g of crude bromide, which was added in 1 hour at 2-5° to a solution of sodioacetoacetic ester, prepared from 46 g of sodium metal and 280 g of acetoacetic ester in 600 ml of anhydrous alcohol. The reaction mass was stirred for 2 hours at 2-5°, then 3 hours at room temperature, and finally 3 hours at 60-65° with simultaneous removal of the alcohol by distillation under slight vacuum. The residue was treated with 1 liter of 10% sodium hydroxide solution and the mixture stirred for 3 hours at 60-65°. Then the mixture was cooled and acidified with concentrated hydrochloric acid (to Congo), the product extracted with ether, and the ether extract washed with bicarbonate solution, then with water, and dried over magnesium sulfate. After removal of the ether by distillation we obtained 226 g of geranylacetone (58%, based on linalool).

B.p. 133-135° (20 mm), n_D^{20} 1.4664, d_4^{20} 0.8696, MR 61.93; calculated. 61.34.

Found %: C 80.05, 80.07; H 11.35, 11.50. $C_{13}H_{22}O$. Calculated %: C 80.34; H 11.41.

The semicarbazone had m.p. 93-94° (from 60% ethanol) [8].

b) A stream of 38.5 g (5.5% excess) of hydrogen chloride was passed in 1 hour with ice-water cooling into 154 g of linalool. After holding at room temperature for 3 hours the aqueous layer (18 ml) was separated, and the chloride was washed quickly with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 158 g of crude chloride, which was added in 40 minutes at 5-7° to a solution of sodioacetoacetic ester, prepared from 23 g of sodium metal and 140 g of acetoacetic ester in 300 ml of anhydrous alcohol The reaction mass was stirred for 2 hours at 5-7°, then for 4 hours at room temperature, and finally for 3 hours at 60-65° with simultaneous removal of the alcohol by distillation under slight vacuum. The residue was treated with 500 ml of 10% sodium hydroxide solution, the mixture stirred for 3 hours at 60-65°, and then worked up in the same manner as described above.

We obtained 111 g (57%, based on linalool) of geranylacetone with b.p. 132-134° (19 mm), n_D^{20} 1.4664.

Method B. A mixture of 462 g of linalool and 1170 g of acetoacetic ester was heated for 3 hours at 120-198°. Here 170 ml of liquid with b.p. 60-82° distilled and 57 liters (84.5%) of carbon dioxide was evolved. After removal of the excess acetoacetic ester (720 g) by distillation the residue was washed with bicarbonate solution, then with water, and finally dried over magnesium sulfate. Fractional distillation in vacuo gave 375 g (64.5%) of geranylacetone with b.p. 120-122° (10 mm), n_D^{20} 1.4666. Carroll, the first to run this reaction (in the presence of sodium ethylate), obtained a 41% yield of geranylacetone [4].

Method C. One gram of anhydrous pyridine and 35 g of diketene were added in 20 minutes to 54 g of linalool with stirring and water cooling. The mixture was stirred for 3 hours at room temperature, 2 hours at 70°, and then it was heated for 30 minutes at 140-195°. Here 6.1 liters (78%) of carbon dioxide was liberated. The residue was washed with bicarbonate solution, then with water, and finally dried over magnesium sulfate. Fractional distillation gave 38.5 g (56.5%) of geranylacetone with b.p. 133-135° (20 mm), n_D^{20} 1.4666. This reaction was first run by Kimel and Cope [5], who obtained a 47.5% yield of geranylacetone in this manner.

Preparation of dehydronerolidol (VII). A mixture of 2.5 liters of ether and 112 g of potassium hydroxide was charged into a steel reactor, acetylene was introduced to a pressure of 7 atm, and then 320 g of geranylacetone was added in 1 hour at 0°. The reaction mass was stirred at 0.5° for 2 hours and at room temperature for 3 hours. Then 250 ml of water was added, the mixture stirred for 15 minutes, and the product worked up in the same manner as described above for the synthesis of dehydrolinalool. We obtained 338 g (93%) of dehydronerolidol [17].

B.p. 117-119° (0.6 mm), n_D^{20} 1.4798, d_4^{20} 0.8886, MR 70.31; calculated 70.06.

Found %: C 81.60 81.70; H 10.94, 11.10. $C_{15}H_{20}O$. Calculated %: C 81.81. H 10.91.

Preparation of nerolidol (VIII). For this 130 g of dehydronerolidol was hydrogenated in the presence of 0.25 g of palladium catalyst, deposited on calcium carbonate. In 3 hours 14.05 liters (17°, 746 mm) of hydrogen was absorbed and the acetylenic bond had disappeared. We obtained 126.1 g (96.4%) of nerolidol [17].

B.p. 94° (0.18 mm), n_D^{20} 1.4784, d_4^{20} 0.8752, MR 71.86; calculated 71.60

Found %: C 80.88, 80.80; H 11.79, 11.83. $C_{15}H_{26}O$. Calculated %: C 81.08, H 11.71.

Isomerization of nerolidol to farnesol (IX). A stream of 43 g (6% excess) of gaseous hydrogen bromide was passed in 1 hour with ice-water cooling into a mixture of 111 g of nerolidol and 100 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (9 ml) was separated, the bromide washed quickly with cold bicarbonate solution, then with water, dried over magnesium sulfate, and the isooctane vacuum-distilled. We obtained 138 g of crude bromide, which was added in 30 minutes at room temperature to a solution of 50 g of potassium acetate in 500 ml of dimethylformamide (the potassium acetate failed to dissolve completely). The mixture was stirred at room temperature for 3 hours and at 55-60° for 2 hours. The precipitate of potassium bromide (60 g) was filtered, the dimethylformamide was vacuum-distilled, and the residue was treated with 300 ml of 10% potassium hydroxide solution.

The mixture was stirred for 4 hours at 65-70°, and the product was worked up in the same manner as described above in the experiment on the isomerization of linalool. We obtained 70 g of farnesol with b.p. 108-112° (0.18 mm), n_D^{20} 1.4868. After purification by chromatographing on aluminum oxide we obtained 67 g of pure farnesol [18] (60%, based on nerolidol).

B.p. 126-127° (0.5 mm), n_D^{20} 1.4872, d_4^{20} 0.8886, MR 72.02; calculated 71.60.

Found %: C 81.14, 81.27; H 11.69, 11.56. $C_{15}H_{26}O$. Calculated %: C 81.08; H 11.71.

Preparation of farnesylacetone (X). Method A. a) Four grams (11% excess) of hydrogen chloride was passed in 30 minutes with ice-water cooling into a solution of 22.2 g of nerolidol in 20 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.6 ml) was separated, the chloride washed quickly with bicarbonate solution, then with water dried over magnesium sulfate, and the isooctane vacuum-distilled. The crude chloride was then added in 20 minutes at 5-7° to a solution of sodioacetoacetic ester, prepared from 2.3 g of sodium metal and 14 g of acetoacetic ester in 100 ml of anhydrous methanol. The mixture was stirred for 3 hours at room temperature and for 2 hours at 60° with simultaneous removal of the methanol by distillation under slight vacuum. The residue was treated with 70 ml of 10% potassium hydroxide solution, the mixture stirred for 2 hours at room temperature, then for 2 hours at 50-55°, and finally it was worked up in the usual manner. We obtained 14.6 g of farnesylacetone [7] (55.7%, based on nerolidol).

B.p. 143-144° (0.42 mm), n_D^{20} 1.4810, d_4^{20} 0.8904, MR 83.87; calculated 83.93.

Found %: C 82.27, 82.40; H 11.58, 11.56. $C_{18}H_{30}O$. Calculated %: C 82.38; H 11.52.

The semicarbazone had m.p. 81.5-82° (from 60% ethanol) [9].

Method B. A mixture of 55 g of nerolidol and 98 g of acetoacetic ester was heated for 2 hours at 140-190°. Here 22 ml of liquid with b.p. 60-76° distilled and 4.8 liters (84%) of carbon dioxide was evolved. After removal of the excess acetoacetic ester by distillation the residue was washed with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 41.6 g (63%) of farnesylacetone with b.p. 156-158° (1 mm), n_D^{20} 1.4814.

Method C. A mixture of 22.2 g of nerolidol, 9.5 g of diketene and 0.5 g of pyridine was stirred for 3 hours at room temperature, for 2 hours at 60°, and then heated for 30 minutes at 140-195°. Here 1.64 liters (72.5%) of carbon dioxide was evolved. The residue was treated with bicarbonate solution, then with water, and dried over magnesium sulfate. We obtained 15.8 g (60%) of farnesylacetone with b.p. 120-123° (0.18 mm), n_D^{20} 1.4808.

Preparation of geranyldehydrolinalool (XI). A mixture of 1 liter of absolute ether, 25 g of powdered potassium hydroxide and 10 ml of ethanol was charged into a steel reactor. Then 60 g of farnesylacetone was added in 30 minutes at 0° and an acetylene pressure of 9 atm. The mixture was stirred at room temperature for 5 hours, the acetylene vented, 50 ml of water added, the mixture stirred for 15 minutes, and the product worked up in the usual manner. We obtained 58.5 g (89%) of geranyldehydrolinalool [7].

B.p. 144-145° (0.3 mm), n_D^{20} 1.4892, d_4^{20} 0.8952, MR 93.07; calculated 92.68.

Found %: C 83.23, 83.41; H 11.14, 11.24. $C_{20}H_{32}O$. Calculated %: C 83.27; H 11.18.

Preparation of geranyllinalool (XII). A solution of 55 g of geranyldehydrolinalool in 100 ml of methanol was hydrogenated in the presence of Pd-catalyst. In 2 hours 4.5 liters (20°, 748 mm) of hydrogen was absorbed and the test for acetylenic hydrogen became negative. We obtained 50.2 g (91%) of geranyllinalool [7].

B.p. 144-146° (0.32 mm), n_D^{20} 1.4874, d_4^{20} 0.8852, MR 94.39; calculated 94.21.

Found %: C 82.33, 82.00; H 12.07, 12.04. $C_{20}H_{34}O$. Calculated %: C 82.69; H 11.80.

Isomerization of geranyllinalool to geranylgeraniol (XIII). Six grams (7% excess) of hydrogen bromide was passed in 30 minutes with ice-water cooling into a solution of 20 g of geranyllinalool in 50 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.2 ml) was separated, the bromide washed quickly with cold bicarbonate solution, then with water, dried over magnesium sulfate, and the isooctane vacuum-distilled. The obtained bromide was added in 10 minutes to a solution of 7 g of potassium acetate in 150 ml

of dimethylformamide. The mixture was stirred for 3 hours at room temperature and for 2 hours at 60-65°. The precipitate of potassium bromide (8.5 g) was filtered, the dimethylformamide was vacuum-distilled, and the residue was treated with 60 ml of 10% potassium hydroxide solution. The mixture was stirred for 4 hours at 60-65° and the product was worked up in the usual manner. We obtained 16.1 g of geranylgeraniol with b.p. 160-165° (0.32 mm), which after purification by chromatographing on aluminum oxide gave 14.6 g (73%) of pure geranylgeraniol [7].

B.P. 162-164° (0.32 mm), n_D^{20} 1.4948, d_4^{20} 0.8922, MR 94.75; calculated 94.21.

Found %: C 82.60, 82.38; H 11.87, 11.91. $C_{20}H_{34}O$. Calculated %: C 82.69; H 11.80.

Preparation of methylheptanone (XIV). a) To a solution of sodioacetoacetic ester, obtained from 85 g of sodium metal and 470 ml of acetoacetic ester in 1000 ml of methanol, was added 646 g of isoamyl iodide. The mixture was stirred for 4 hours at room temperature and for 5 hours at 64°. The methanol was distilled off and the residue was saponified with 15% sodium hydroxide solution at the boil for 6 hours. Then the mixture was cooled and acidified with concentrated hydrochloric acid, after which the product was extracted with ether, washed with saturated bicarbonate solution, then with water, and dried over calcium chloride. The ether was distilled off and the residue was vacuum-distilled to give 240 g (47%) of methylheptanone with b.p. 41-42° (6 mm), n_D^{20} 1.4135.

b) The hydrogenation of 696 g of methylheptenone (II) was run in a steel autoclave at room temperature in the presence of 1.5 g of platinum oxide and a hydrogen pressure of 100-20 atm. In 6 hours the hydrogen absorption was 140 liters (theory is 134 liters of hydrogen). The test with tetranitromethane did not give a yellow color. The catalyst was filtered and the residue was vacuum-distilled. We obtained 600 g (86%) of methylheptanone with b.p. 46.5-48° (7 mm), n_D^{20} 1.4144.

The semicarbazone had m.p. 154-155° (from aqueous methanol) [20].

Preparation of 3,7-dimethyl-1-octyn-3-ol (XV). A mixture of 3.5 liters of absolute ether, 400 g of powdered potassium hydroxide and 20 ml of ethanol was charged into a 6-liter steel autoclave. After purging the system with nitrogen the reaction mass was saturated with acetylene to a pressure of 7 atm, and then 500 g of methylheptanol was added in 1 hour at 8-10°. The reaction mass was stirred for another 3 hours, the excess acetylene removed, 800 ml of water added, and after stirring for 15 minutes the product was worked up in the usual manner. We obtained 524 g (87%) of 3,7-dimethyl-1-octyn-3-ol with b.p. 69-71° (7 mm), n_D^{20} 1.4398.

Found %: C 77.46, 77.45; H 11.64, 11.63. $C_{10}H_{18}O$. Calculated %: C 77.88; H 11.73.

3,5-Dinitrobenzoate, m.p. 79.5-80.5°.

Found %: N 8.33, 8.61. $C_{17}H_{20}O_6N_2$. Calculated %: N 8.05.

Preparation of 3,7-dimethyl-1-octen-3-ol (dihydrolinalool) (XVI). The hydrogenation of 246 g of 3,7-dimethyl-1-octyn-3-ol at atmospheric pressure in the presence of Pd-catalyst on calcium carbonate (5% palladium content) until 38.5 liters of hydrogen was absorbed required 4 hours. Theory for hydrogen absorption is 38.6 liters. The end of hydrogenation was determined by the acetylenic test with ammoniacal silver nitrate solution. The catalyst was filtered, and the product was vacuum-distilled. We obtained 222 g (90%) of 3,7-dimethyl-1-octen-3-ol [21] with b.p. 68-70 (6 mm), n_D^{20} 1.4390.

Found %: C 76.35, 76.55; H 13.32, 13.14. $C_{10}H_{20}O$. Calculated %: C 76.65; H 12.90.

Preparation of 3,7-dimethyl-3-octanol (tetrahydrolinalool). A solution of 26.4 g of 3,7-dimethyl-1-octen-3-ol in methanol was hydrogenated over platinum oxide at atmospheric pressure. Here 3.9 liters of hydrogen was absorbed. The calculated amount of hydrogen is 4.15 liters. The catalyst was filtered, and the filtrate was fractionally distilled in vacuo. We obtained 25.5 g of 3,7-dimethyl-3-octanol.

B.p. 71-73° (6mm), n_D^{20} 1.4331, d_4^{20} 0.8294, MR 49.62; calculated 49.90.

The 3,5-dinitrobenzoate had m.p. 45.5-46.5°.

Found %: C 57.86, 58.02; H 6.96, 6.94; N 8.02, 8.07. $C_{17}H_{24}O_6N_2$. Calculated %: C 58.01; H 6.87; N 7.95.

Preparation of 6,10-dimethyl-5-undecen-2-one (tetrahydropseudoionone) (XVII). Method A. a) A stream of 3.8 g (5% excess) of hydrogen chloride was passed with ice-water cooling into a solution of 15.6 g of 3,7-

-dimethyl-1-octen-3-ol in 25 ml of isooctane. After holding at room temperature for 2 hours the aqueous layer (1.7 ml) was separated, the chloride washed with saturated sodium bicarbonate solution, then with water, and dried over magnesium sulfate.

Without further purification the obtained chloride was added in 20 minutes at −13° to a solution of sodioacetoacetic ester, obtained from 2.4 g of sodium metal and 14 ml of acetoacetic ester in 50 ml of methanol. The mixture was stirred for 2 hours at from −13° to 0°, then for 2 hours at 18°, and the next day for another 5 hours at 50°. A solution of 7 g of sodium hydroxide in 60 ml of water was then added to the reaction mass and the whole stirred for 5 hours at 60-65°. The mixture after cooling was acidified with concentrated hydrochloric acid, the product extracted with ether, and the ether extract washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate. After removal of the ether by distillation and vacuum-distillation of the residue we obtained 11.8 g (60%) of tetrahydropseudoionone with b.p. 83-85° (2 mm), n_D^{20} 1.4472.

b) A stream of 144 g (6% excess) of hydrogen bromide was passed with ice-salt cooling into a solution of 257 g of 3,7-dimethyl-1-octen-3-ol in 100 ml of isooctane. After holding for 5 hours at room temperature the aqueous layer (32 ml) was separated, the bromide washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate.

Without further purification the obtained bromide was added in two hours to a −13° solution of sodioacetoacetic ester, obtained from 40 g of sodium metal and 240 ml of acetoacetic ester in 600 ml of methanol. The mixture was then stirred for 5 hours at from −13 to + 18° and allowed to stand overnight. The next day the mixture was stirred for another 5 hours at 60°, 2/3 of the methanol was distilled under slight vacuum, and the residue was saponified with a solution of 120 g of sodium hydroxide in 900 ml of water for 5 hours at 70° After cooling, the product was acidified with concentrated hydrochloric acid and worked up in the usual manner.

We obtained 239 g (74%) of tetrahydropseudoionone with b.p. 75-77° (1 mm), n_D^{18} 1.4498.

Method B. A mixture of 184.7 g of 3,7-dimethyl-1-octen-3-ol and 450 ml of acetoacetic ester was heated for 1 hour at 160-210°. Here 16 liters (68%) of carbon dioxide was evolved. The excess acetoacetic ester was distilled off, and the residue was washed 3 times with 10% sodium bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 129.0 g (60%) of tetrahydropseudoionone with b.p. 84-85° (1 mm), n_D^{20} 1.4481.

Found %: C 79.10, 79.00; H 12.30, 12.20. $C_{13}H_{24}O$. Calculated %: C 79.52; H 12.32.

Both the semicarbazone and the 2,4-dinitrophenylhydrazone melted at room temperature.

Method C. Diketene (17.5 g) and 10 drops of anhydrous pyridine were added to 23.4 g of 3,7-dimethyl--1-octen-3-ol. The temperature of the reaction mixture rose from 20 to 36°. The mixture was stirred for 7 hours, allowed to stand overnight, then stirred for another hour at 60-80°, cooled, washed with 10% sodium bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 30.6 g of the acetoacetate of 3,7-dimethyl-1-octen-3-ol with b.p. 98-100° (1 mm), n_D^{20} 1.4462.

The obtained acetoacetate was pyrolyzed at 180-198°. Here 1880 ml of carbon dioxide was evolved in 1.5 hours. Fractional distillation in vacuo gave 12.1 g (41%) of 6,10-dimethyl-5-undecen-2-ol with b.p. 84-85° (1 mm), n_D^{20} 1.4478.

Preparation of 6,10-dimethyl-2-undecanone (hexahydropseudoionone) (XVIII). The hydrogenation of 227 g of tetrahydropseudoionone was run in a steel autoclave at room temperature over a mixed catalyst composed of 1.2 g of PtO_2 and 1 g of $Pd/CaCO_3$. Here 29 liters of hydrogen was absorbed in 7 hours at a hydrogen pressure of 100-20 atm. Calculated amount is 27.9 liters. Fractional distillation in vacuo gave 208 g (90%) of hexahydropseudoionone with b.p. 95-97° (4 mm), n_D^{20} 1.4334.

The semicarbazone had m.p. 95-96° (from aqueous methanol) [22].

Preparation of 3,7,11-trimethyl-1-dodecyn-3-ol (XIX). A mixture of 4 liters of absolute ether and 350 g of powdered potassium hydroxide was charged into a steel reactor and after purging with nitrogen the mixture was saturated with acetylene to a pressure of 10 atm. Then 246 g of hexahydropseudoionone was added in 1.2 hours at −10°, after which the mixture was stirred for 1 hour at −10°, and for 2 hours without cooling. After the usual treatment we obtained 247 g (89%) of 3,7,11-trimethyl-1-dodecyn-3-ol with b.p. 96-98° (1 mm), n_D^{20} 1.4492.

Found %: C 80.17, 80.02; H 12.67, 12.47. $C_{15}H_{28}O$. Calculated % C 80.24; H 12.62.

The 3,5-dinitrobenzoate had m.p. 47.5-48.5°

Found %: C 63.17, 63.13; H 7.20, 7.20; N 6.99, 7.10. $C_{22}H_{30}O_6N_2$. Calculated %: C 63.13; H 7.22; N 6.69.

Preparation of 3,7,11-trimethyl-1-dodecen-3-ol (XX). The hydrogenation of 119.6 g of 3,7,11-trimethyl--1-dodecyn-3-ol was run at atmospheric pressure in the presence of 0.2 g of Pd/$CaCO_3$. The hydrogenation was stopped when 12.5 liters of hydrogen had been absorbed and the acetylenic test was negative. The calculated amount of hydrogen is 13 liters. The catalyst was filtered and the filtrate was fractionally distilled in vacuo. We obtained 113.1 g (94%) of 3,7,11-trimethyl-1-dodecen-3-ol with b.p. 123-125° (6 mm), n_D^{20} 1.4490.

Found %: C 78.96, 79.01; H 13.31, 13.41. $C_{15}H_{30}O$. Calculated %: C 79.64; H 13.36.

The 3,5-dinitrobenzoate is a liquid.

Hydrogenation of 3,7,11-trimethyl-1-dodecen-3-ol. The hydrogenation of 12.4 g of 3,7,11-trimethyl--1-dodecen-3-ol was run over platinum oxide at atmospheric pressure. Here 1.30 liters of hydrogen was absorbed. The calculated amount of hydrogen is 1.33 liters. After fractional distillation in vacuo we obtained 10 g of 3,7,11-trimethyl-3-dodecanol.

B.p. 127-130° (7 mm), n_D^{20} 1.446, d_4^{20} 0.8387, MR 72.44; calculated 72.99.

Found %: C 78.46, 78.47; H 14.11, 14.00. $C_{15}H_{32}O$. Calculated %: C 78.89; H 14.09.

The 3,5-dinitrobenzoate is a liquid.

Preparation of 6,10,14-trimethyl-5-pentadecen-2-one (XXI). Method A. a) A stream of 10.1 g (20% excess) of dry hydrogen bromide was passed without cooling into a solution of 22.6 g of 3,7,11-trimethyl-1--dodecen-3-ol in 22 ml of isooctane. After holding at room temperature for 3 hours the aqueous layer was separated, and the bromide washed with saturated bicarbonate solution, then with water, and dried over magnesium sulfate.

The crude bromide was added to a −10° solution of sodioacetoacetic ester, prepared from 2.3 g of sodium metal and 14 ml of acetoacetic ester in 60 ml of methanol. The mixture was stirred for 2 hours at −10°, for 2 hours at 0°, and then allowed to stand overnight at room temperature. The next day the mixture was stirred for 2 hours at 60° and then treated with a solution of 7 g of sodium hydroxide in 60 ml of methanol. After this the mixture was stirred at 60-70° for 4 hours, 2/3 of the methanol was distilled off, the residue diluted with water, then acidified with hydrochloric acid, and after the usual treatment we obtained 12.5 g (49%) of 6,10,14-trimethyl-5-pentadecen-2-one with b.p. 121-125° (1 mm), n_D^{20} 1.4560.

Method B. A mixture of 45.6 g of 3,7,11-trimethyl-1-dodecen-3-ol and 100 ml of acetoacetic ester was heated at 170-188°. The copious evolution of carbon dioxide continued for 1.5 hours. When gas evolution had ceased the excess acetoacetic ester was distilled off, and the residue was washed with bicarbonate solution, then with water, and dried over magnesium sulfate. Two fractional distillations in vacuo gave 35.7 g (65%) of 6,10,14-trimethyl-5-pentadecen-2-one.

B.p. 132-137° (1.5 mm), n_D^{20} 1.4545.

Found %: C 80.92, 80.85; H 12.62, 12.74. $C_{18}H_{34}O$. Calculated %: C 81.12; H 12.86.

Both the semicarbazone and 2,4-dinitrophenylhydrazone melted below room temperature.

Method C. Ten grams of diketene was added in 10 minutes with stirring to a mixture of 14.3 g of 3,7,11-trimethyl-1-dodecen-3-ol and 10 drops of anhydrous pyridine. The temperature of the reaction mass rose from 15 to 35°. The product was allowed to stand overnight, and the next day was subjected to pyrolysis at 130-190°. Here 1.10 liters of carbon dioxide was evolved in 30 minutes (theory is 1.42 liters). The residue was washed with 10% bicarbonate solution, then with water, and dried over magnesium sulfate. Fractional distillation in vacuo gave 7.8 g of 6,10,14-trimethyl-5-pentadecen-2-one with b.p. 127-135° (1 mm), n_D^{20} 1.4545. After chromatographing on aluminum oxide we obtained 3.2 g of pure ketone (XXI) [23] with b.p. 129-130° (1 mm), n_D^{20} 1.4541.

Preparation of 6,10,14-trimethyl-2-pentadecanone (XXII). The hydrogenation of 30 g of 6,10,14-trimethyl-5-pentadecen-2-one was run at atmospheric pressure in the presence of 0.75 g of platinum oxide. Here 2.62 liters of hydrogen were absorbed in 5 hours. The calculated amount of hydrogen is 2.68 liters. After filtration and fractional distillation in vacuo we obtained 28.5 g (95%) of 6,10,14-trimethyl-2-pentadecanone with b.p. 120-123° (1 mm), n_D^{20} 1.4445.

The semicarbazone had m.p. 69-70° [10, 24].

Preparation of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol (isophytol) (XXIII). 6,10,14-Trimethyl-2-pentadecanone (48.8 g) was added in thirty minutes to a −15° mixture of 600 ml of absolute ether, 60 g of powdered potassium hydroxide and 10 ml of anhydrous methanol, saturated with acetylene to a pressure of 12 atm. The mixture was stirred for 1 hour at −15° and then for 2 hours without cooling. After the usual treatment we obtained 47.7 g (90%) of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol.

B.p. 122-125° (0.06 mm), n_D^{20} 1.4543, d_4^{20} 0.8525, MR 93.58; calculated 94.02.

Found %: C 81.75, 81.86; H 12.92, 13.16. $C_{20}H_{38}O$. Calculated %: C 81.50; H 13.01.

The 3,5-dinitrobenzoate is a pale yellow liquid.

Preparation of 3,7,11,15-tetramethyl-1-hexadecen-3-ol (XXIV). The hydrogenation of 39.0 g of 3,7,11,15-tetramethyl-1-hexadecyn-3-ol was run at atmospheric pressure in the presence of 0.06 g of $Pd/CaCO_3$. Here 3082 ml of hydrogen was absorbed in 2 hours, after which the acetylenic test showed negative. The calculated amount of hydrogen is 3240 ml. The catalyzate was filtered and the filtrate was fractionally distilled in vacuo. We obtained 36.8 g (84%) of 3,7,11,15-tetramethyl-1-hexadecen-3-ol.

B.p. 125-128° (0.06 mm), n_D^{20} 1.4546, d_4^{20} 0.8459, MR 95.04; calculated 95.61.

Found %: C 80.80, 80.82; H 13.43, 13.68. $C_{20}H_{40}O$. Calculated %: H 81.02; H 13.42

SUMMARY

We worked out in detail the total synthesis of the isoprenoid alcohols linalool, geraniol, nerol, nerolidol, farnesol, geranyllinalool, geranylgeraniol and phytol, and also of the intermediate products of this synthesis, namely ketones and acetylenic alcohols, employing the successive repetition of the reactions of condensation of ketones with acetylene, selective hydrogenation of acetylenic alcohols, and conversion of tertiary vinyl alcohols to the isomeric primary alcohols of allylic type and unsaturated ketones of the allylacetone type.

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SIMPLER ANALOGS FOR CORTICOSTEROIDS

I. STEREOCHEMISTRY OF CYANOHYDRIN AND ACETYLENIC SYNTHESIS. CONFIGURATION OF 1-CYANO- AND 1-ETHYNYL-2-METHYLCYCLOHEXANOLS

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The condensation of 2-methylcyclohexanone (I) with hydrogen cyanide and with acetylene yields in each case two stereoisomeric (crystalline and liquid) cyanohydrins (II, III) [1, 2] and acetylenic alcohols (IV, V) [3], the configuration of which, however, has not been established until now.

It seemed of interest to us to establish the spatial structure of these compounds and to trace the stereochemical course of the cyanohydrin and acetylenic syntheses in a number of substituted cyclohexanones. Of even greater interest here is the fact that studies, devoted to the stereochemistry of nucleophilic additions, do not exist in the indicated series.

To obtain crystalline derivatives of cyanohydrins (II) and (III) it seemed most convenient to saponify the nitriles to hydroxy acids, since crystalline derivatives of the cyanohydrins based on the hydroxy group cannot be obtained. However, the saponification of cyanohydrins (II) and (III) proceeds with difficulty and cannot be accomplished under ordinary conditions [2, 4, 5]. Drastic reaction conditions cause decomposition of the cyanohydrins and the regeneration of 2-methylcyclohexanone (I) [5].

Welvart [6] described the saponification of a mixture of cyanohydrins (II) and (III) in acetic acid saturated with hydrogen chloride at 20° for 7 days, followed by removal of the acetic acid by steam-distillation. Here a saponification product with m.p. 105° was obtained in 70% yield, which the author assumed was a mixture of the isomeric hydroxy acids.

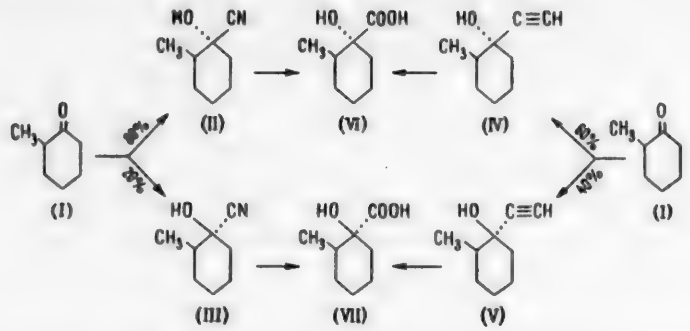
We improved on the Welvart method, replacing the steam-distillation by a boiling of the reaction mass, followed by its evaporation in vacuo, and heating the residue with aqueous soda solution to decompose the unsaponified cyanohydrin. With such a procedure we obtained a nearly quantitative yield of 2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 110-111° from the crystalline cyanohydrin (II) with m.p. 53-54°, while from the liquid isomer (III) we obtained 2-methylcyclohexanol-1-carboxylic acid (VII) with m.p. 94-95°. The liquid cyanohydrin (III) is saponified with greater difficulty and requires a longer reaction time than does the crystalline isomer (II).

When the crystalline 1-ethynyl-2-methylcyclohexanol (IV) with m.p. 56-57° was oxidized with potassium permanganate we again obtained the high-melting hydroxy acid (VI) with m.p. 110-11° [3], while from the liquid 1-ethynyl-2-methylcyclohexanol (V) we obtained the low-melting hydroxy acid (VII) with m.p. 94-95°. Consequently, the formation in the cyanohydrin synthesis of two isomeric 2-methylcyclohexanone cyanohydrins (II) and (III) and their configurative relationship to acetylenic alcohols (IV) and (V) was shown.

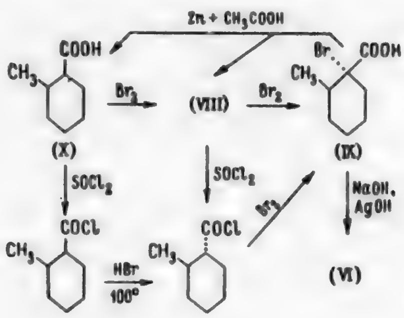
Of the two hydroxy acids obtained (VI) and (VII), only the hydroxy acid (VI) with m.p. 110° was known before. Zernov [7] first obtained it by the bromination of trans-hexahydro-o-toluic acid (VIII) in the presence

* Deceased.

of red phophorus, followed by saponification of the obtained α-bromohexahydro-o-toluic acid (IX) with m.p. 97° using aqueous caustic. This same hydroxy acid was also obtained later by other investigators [3, 8, 9], who however failed to give any indication as to its configuration.



We decided to attempt the preparation of both of the isomeric α-bromohexahydro-o-toluic acids, so that by cross-saponification and on the basis of studying the stereochemistry of the bromination and reduction we could establish the spatial structure of the compounds (II-IV) and (III-V) in which we were interested. However, it proved that when the cis- and trans-hexahydro-o-toluic acids (VIII) and (X) were brominated by the Volhard-Zelinskii method only the α-bromo acid (IX), identical with the acid obtained by Zernov [7], was formed. By means of special experiments it was shown that this reaction goes through the preliminary isomerization of cis-acid (X) to the bromide of trans-acid (VIII). The saponification of bromo acid (IX), either with aqueous caustic or with moist silver oxide, leads to the same hydroxy acid (VI) with m.p. 110-111°, which indicates [10] that apparently the latter and bromo acid (IX) have the same spatial structure.



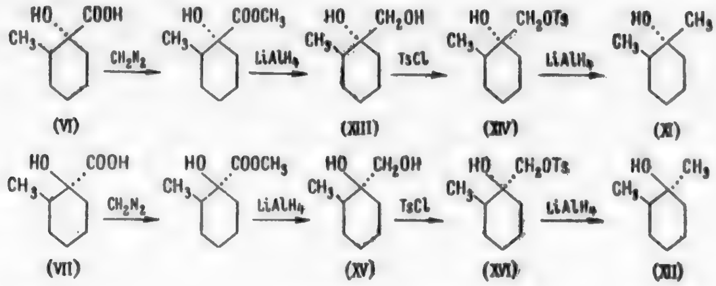
The reduction of bromo acid (IX) with zinc in acetic acid gave a mixture of the isomeric hexahydro-o--toluic acids (VIII) and (X).

As a result, the bromination of trans-acid (VII), or of its chloride, apparently proceeds with inversion of the configuration, while saponification of the α-bromo acid (IX), either with alkali or with moist silver oxide, proceeds without inversion of the configuration.

The configuration of cyanohydrins (II) and (III) and acetylenic alcohols (IV) and (V), obtained from 2--methylcyclohexanone (I), was established by their reduction to the known [11] 1,2-dimethylcyclohexanols (XI) and (XII) without affecting the asymmetric center. To accomplish this the methyl ester of hydroxy acid (VI), obtained using diazomethane, was reduced with aluminum lithium hydride in boiling ether to 1-hydroxymethyl--2-methylcyclohexanol (XIII) with m.p. 64-65°. The latter when treated with toluenesulfonyl chloride in pyridine at 0° was converted to the monotosylate (XIV), which without purification was reduced with aluminum lithium hydride by the Karrer method [12]. With such a procedure hydroxy acid (VI) gave cis-1,2-dimethylcyclohexanol (XI) with m.p. 23-24° and a known configuration [11].

A similar series of transformations was also accomplished with hydroxy acid (VII) with m.p. 94-95°. The liquid diol (XV), obtained from the methyl ester of this acid, gave the crystalline monotosylate (XVI) with m.p.

60-61°, which on reduction with aluminum lithium hydride gave the known trans-1,2-dimethylcyclohexanol (XII) with m.p. 11.5-13° [11]. In both cases the yields in all of the steps were not below 90%, except in the last reaction, where the yield was 75%.

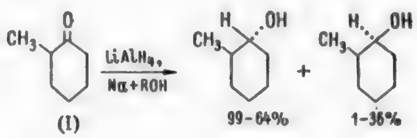


From the obtained experimental results it follows that the crystalline 1-cyano-2-methylcyclohexanol (II) and 1-ethynyl-2-methylcyclohexanol (IV), the same as their derivatives, have the side carbon chains in the cis-position, while the liquid isomers of 1-cyano-2-methylcyclohexanol (III) and 1-ethynyl-2-methylcyclohexanol (V), and also their derivatives, have the carbon chains in the trans-position.

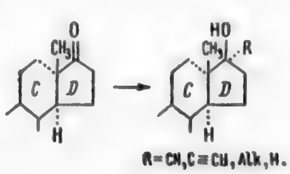
The ratio of the isomeric cyanohydrins (II) and (III), formed in the reaction of 2-methylcyclohexanone (I) with acetone cyanohydrin, was established by saponifying a mixture of the two cyanohydrins, and it proved to be approximately equal to 4 : 1. Consequently, the cyano group adds to 2-methylcyclohexanone (I) preferentially on the side of the methyl substituent.

The condensation of 2-methylcyclohexanone (I) with acetylene in the presence of powdered potassium hydroxide under pressure also proceeds in a similar manner. However, in this case the reaction is less stereospecific and leads to the formation of the isomeric acetylenic alcohols (IV) and (V) in a 3 : 2 ratio.

According to the literature, the ionic reduction of 2-methylcyclohexanone (I) (using aluminum lithium hydride, sodium in alcohols, etc.), which may be regarded as a case of nucleophilic reaction at the carbonyl group [13], also proceeds with a preponderant addition of the hydrogen on the side of the methyl group; the main product obtained here is trans-2-methylcyclohexanol [14, 15].

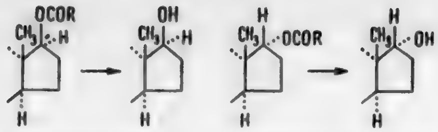


It is well known that in the steroid series the addition of nucleophilic reagents (hydrogen cyanide, acetylene, alkylmagnesium halides, hydrogen, etc.) to 17-keto steroids is stereospecific with a marked preponderance of the 17 β-hydroxy compounds [16].*



In this case the substitutent (R) adds trans to the angular 18-methyl group, i.e. on the side of the largest substituent, which, according to Reichstein [18], is not the angular 18-methyl group but instead the 12-methylene group and the whole ring C. This finds experimental proof also in the greater ease of saponification shown by esters of 17 β-hydroxy steroids [18, 19].

* An exception is the addition of alkylmagnesium halides to D-homo-17 α-keto steroids [17].



Easily saponified Difficultly saponified

As a result, a definite rule is manifested in the stereochemical direction of the ionic addition of acetylene and hydrocyanic acid to a carbonyl group, consisting in the preponderant addition of the entering substituent in the cis-position to the o-alkyl substituent present. The stereochemical direction probably depends on the conditions used to run such reactions.

EXPERIMENTAL

Synthesis of 2-methyl-1-ethynylcyclohexanols (IV) and (V). A mixture of 660 g of powdered potassium hydroxide, 2.5 liters of absolute ether and 10 ml of ethanol was charged into a 6-liter steel reactor, and then with good stirring and cooling the reactor was filled in 30 minutes with acetylene to a pressure of 7 atm. Then 900 g of 2-methylcyclohexanone (b.p. 62-63° at 20 mm, n_D^{17} 1.4499) was added in 6 hours with stirring. The acetylene pressure in the reactor was maintained at 7 atm during the whole experiment. The reaction was run for 10 hours. After removal of the acetylene the product was treated with 800 ml of water with efficient stirring, then neutralized with carbon dioxide, and finally dried over magnesium sulfate. After removal of the ether by distillation the residue was fractionally distilled in vacuo. We obtained 956 g of a liquid mixture of acetylenic alcohols (IV) and (V), with b.p. 76-78° (13 mm) and n_D^{20} 1.4770, and 52 g of an acetylenic glycol. Long freezing of the liquid mixture led to isolation of 450 g of the cis-isomer (IV) with m.p. 56-57° (from petroleum ether) and 450 g of the liquid trans-isomer (V) with b.p. 69-70° (10 mm) and n_D^{17} 1.4780. The liquid isomer (V) contains up to 10% of the crystalline alcohol. The ratio of the crystalline and liquid isomers (IV):(V) is 60 : 40.

Oxidation of cis-1-ethynyl-2-methylcyclohexanol (IV). A solution of 15 g of potassium permanganate in 300 ml of water was added in 3 hours with vigorous stirring to a solution of 10 g of cis-1-ethynyl-2-methylcyclohexanol (IV) (m.p. 56-57°) in 100 ml of acetone, in which connection the temperature was kept below 20°. The mixture was then stirred for another hour at 20° and finally heated for an hour at 100°. The precipitate of manganese dioxide was filtered and washed with hot water. The alkaline solution was evaporated in vacuo to dryness and here 1 g of starting alcohol (IV) with m.p. 56.6-57° was isolated. The residue was washed with ether, acidified with dilute hydrochloric acid, and extracted with ether. After drying the ether extract over sodium sulfate, followed by removal of the ether by distillation, we obtained 3.5 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) as colorless crystals with m.p. 110.5-111° (from benzene) [7-9].

Found %: C 60.51, 60.46; H 8.79, 8.76. $C_8H_{14}O_3$. Calculated %: C 60.76; H 8.86.

Oxidation of trans-1-ethynyl-2-methylcyclohexanol (V). Seventeen grams of trans-1-ethynyl-2-methylcyclohexanol (V) with b.p. 76° (15 mm) was oxidized with 20 g of potassium permanganate at 22-25° in the same manner as in the preceding experiment. On evaporation we obtained 3 g of the starting alcohol and 4.8 g of acid products as a crystallizing oil. Repeated recrystallization of the latter from petroleum ether gave oxalic acid with m.p. 102°, which did not depress the melting point with an authentic specimen, and 0.5 g of trans-2-methylcyclohexanol-1-carboxylic acid (VII) as colorless needles with m.p. 94.5-95°.

Found %: C 60.66, 60.61; H 8.90, 8.84. $C_8H_{14}O_3$. Calculated %: C 60.77; H 8.86.

The mixed melting point of this acid with hydroxy acid (VI) was 72-84°.

Separation of 2-methylcyclohexanone cyanohydrins (II) and (III). The seeding and freezing of 120.5 g of mixed 2-methylcyclohexanone cyanohydrins (II) and (III) with b.p. 95.5-98° (3.5 mm), obtained by reacting 2-methylcyclohexanone with acetone cyanohydrin [1], led to the isolation of 70.5 g of crystalline cis-1-cyano-2-methylcyclohexanol (II) with m.p. 53-54° (from n-heptane) and 49 g of a liquid mixture, rich in trans-1-cyano-2-methylcyclohexanol (III).

Saponification of cis-1-cyano-2-methylcyclohexanol (II). A solution of 14 g of cis-1-cyano-2-methylcyclohexanol (m.p. 53-54°) in 60 ml of glacial acetic acid and 80 ml of concentrated hydrochloric acid was

saturated with hydrogen chloride for 1 hour and then allowed to stand for 7 days at 20°. Then the solution was boiled for 5 hours under reflux, and then evaporated in vacuo. The crystalline residue was dissolved in 150 ml of saturated soda solution and then heated for 3 hours on the boiling water bath, The alkaline solution after cooling was extracted twice with ether and then acidified with dilute hydrochloric acid until strongly acid. Here an oil tending to crystallize was obtained, which was extracted with ether. The water layer was again extracted with ether in a Soxhlet apparatus for 10 hours. From the combined ether extracts, after drying over sodium sulfate and removal of the ether by distillation, we obtained 15.8 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI), which after treatment with petroleum ether and recrystallization from a mixture of chloroform and n-heptane melted at 110-111°, and did not give a melting point depression when mixed with the hydroxy acid (VI) obtained from acetylenic alcohol (IV). If the reaction mass was allowed to stand only one night at 20°, with the rest of the treatment the same as before, the yield of cis-hydroxy acid (VI) was only 9.5 g.

When the hydrochloric acid and hydrogen chloride were replaced by hydrobromic acid and hydrogen bromide, and the mixture allowed to stand for 7 days, we obtained 0.5 g of a dark brown oil, from which we were unable to isolate any crystalline products.

Saponification of liquid mixture of isomeric 1-cyano-2-methylcyclohexanols (II) and (III). a) A treatment similar to the above of 14 g of liquid mixed cyanohydrins, obtained after freezing out the cis-1-cyano--2-methylcyclohexanol (II) with m.p. 53-54° and rich in the trans-isomer (III), gave 12.4 g of mixed hydroxy acids as a crystallizing oil. Recrystallization from petroleum ether gave crystals that melted at 65-80°. Fractional crystallization from petroleum ether and benzene gave 3 g of a hydroxy acid with m.p. 101-104°, which did depress the melting point when mixed with the above described cis-hydroxy acid (VI). We were unable to isolate the trans-hydroxy acid (VII) by crystallization.

b) To obtain a more accurate idea of the ratio of isomeric cyanohydrins (II) and (III), a solution of 14 g of the original mixture of cyanohydrins in 60 ml of glacial acetic acid and 80 ml of concentrated hydrochloric acid was saturated with hydrogen chloride, allowed to stand for 1.5 months at 20°, then boiled under reflux for 8.5 hours, and worked up in the usual manner. We obtained 14.7 g of mixed 2-methylcyclohexanolcarboxylic acids (VI) and (VII) with m.p. 85-93°. Fractional crystallization from a mixture of ether and petroleum ether gave 9.2 g of cis-hydroxy acid (VII) with m.p. 106-109°, which did not depress the melting point when mixed with the preceding specimen. The 5.3 g of oil isolated from the mother liquors was chromatographed on 100 ml of aluminum oxide washed with hydrochloric acid. The product was eluted successively with petroleum ether, benzene, ether, and methanol. From the ether fractions we isolated 0.4 g of trans-hydroxy acid (VII) with m.p. 92-93°, which did not give a melting point depression with the above described specimen, and 2.1 g of an oily mixture of hydroxy acids, also containing a large amount of trans-hydroxy acid (VII). From the methanol fractions we obtained an additional 2.65 g of cis-hydroxy acid (VI) with m.p. 108-110°.

Cis-Δ^3-2-methylcyclohexenecarboxylic acid. A mixture of 470 g of acrylic acid (b.p. 140-141°), obtained by the Kaszuba method [20], and 750 ml of trans-piperylene was heated in the presence of hydroquinone in a 2-liter autoclave at 130° for 6 hours. After 2 vacuum-distillations we obtained 590 g of condensation product with b.p. 102-104° (2 mm). By freezing, followed by recrystallization from petroleum ether, we isolated 177.2 g of cis-Δ^3-2-methylcyclohexenecarboxylic acid with m.p. 62-63° [21].

Hydrogenation of cis-Δ^3-2-methylcyclohexenecarboxylic acid. A solution of 70 g of cis-Δ^3-2-methylcyclohexenecarboxylic acid in 200 ml of glacial acetic acid was hydrogenated over platinum oxide at 20° and atmospheric pressure. In 8 hours 11.7 liters of hydrogen was absorbed. The catalyst was filtered and the product was fractionally distilled in vacuo. We obtained 67 g of cis-2-methylcyclohexanecarboxylic acid (X) with b.p. 98-100° (3 mm), n_D^{20} 1.4641 [22].

The anilide of the acid, recrystallized from benzene had m.p. 127-128° [21, 22].

Found %: N 6.48, 6.56. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Similar results were obtained when the hydrogenation was run in 95% alcohol.

Bromination of cis-2-methylcyclohexanecarboxylic acid (X). Fourteen grams of bromine was added in drops with stirring to a mixture of 7.1 g of cis-2-methylcyclohexanecarboxylic acid and 0.4 g of red phosphorus. When exothermic reaction had ceased the mixture was heated on the water bath at 54-56° for 3 hours, then for 2 hours at 100°, and finally it was allowed to stand overnight at 20°. The next day the reaction mass was washed

with water and then heated with 2 volumes of formic acid (85%) on the boiling water bath for 15 minutes. The mixture was evaporated in vacuo, diluted with ether, and washed with water. After drying the ether solution over sodium sulfate, followed by removal of the ether by distillation, we obtained 11.1 g of a crystallizing oil, from which we isolated 6.5 g of crystalline 1-bromo-2-methylcyclohexanecarboxylic acid (IX) with m.p. 95-96.5° (from petroleum ether) [7].

Found %: C 43.39, 43.38; H 5.94, 5.93; Br 36.57, 36.48. $C_8H_{13}O_2Br$. Calculated %: C 43.43; H 5.93; Br. 36.11.

Reaction of bromine with cis-2-methylcyclohexanecarboxylic acid (X). Twelve grams of bromine was added with water cooling to 17.04 g of cis-2-methylcyclohexanecarboxylic acid, after which the mixture was allowed to stand for 2 hours at 20°, and then it was heated for 2 hours at 100°. Fractional distillation in vacuo gave 11 g of trans-2-methylcyclohexanecarboxyl bromide with b.p. 70-76° (5 mm). When this bromide (2.6 g) was treated with aniline (2.5 ml) in absolute benzene (10 ml) we obtained 2.8 g of the anilide of trans-2-methylcyclohexanecarboxylic acid with m.p. 152-153.5° (from benzene) [7,21, 22, 23].

Found %: N 6.27, 6.13. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Reaction of thionyl chloride with cis-2-methylcyclohexane-carboxylic acid (X). A mixture of 19.2 g of cis-2-methylcyclohexanecarboxylic acid and 10 ml of thionyl chloride was kept at 20° for 1 hour, then heated for 1 hour at 100°, and finally allowed to stand overnight. The anilide, obtained from a test sample, had m.p. 126-127° (from benzene) and did not depress the mixed melting point with the anilide of authentic cis-2-methylcyclohexanecarboxylic acid [21, 22]. After heating the reaction mass at 100° for hours in a stream of dry hydrogen bromide the anilide obtained from a test sample had m.p. 151-152° (from benzene) and did not give a melting point depression with the anilide of trans-2-methylcyclohexanecarboxylic acid. When a test sample of the acid chloride was treated with aqueous caustic solution, followed by acidification and extraction with ether, we obtained trans-2-methylcyclohexanecarboxylic acid (VIII) with m.p. 51-52° (from petroleum ether) [7, 21]. The remainder of the reaction mass (about 18 g) was treated with 21.6 g of bromine and the mixture was first heated for 1 hour at 80° and then for 2 days at 100°, after which it was treated with two volumes of formic acid at 100° for 15 minutes. The formic acid was vacuum-distilled, while the residue was dissolved in ether and washed with water. After drying over sodium sulfate and removal of the ether by distillation we obtained 23.9 g of a crystallizing oil, from which we isolated 9.5 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) with m.p. 95-97°, which did not depress the melting point when mixed with the specimen described above.

Saponification of 1-bromo-2-methylcyclohexanecarboxylic acid (IX). a) 1-Bromo-2-methylcyclohexanecarboxylic acid (2.21 g) was titrated with 0.1 N sodium hydroxide solution in the presence of phenolphthalein. The color began to disappear more slowly after 100 ml of the caustic solution had been added. Then another 212 ml of caustic solution was added and the mixture was allowed to stand overnight, after which the excess alkali was back-titrated with 0.1 N sulfuric acid solution, and this required 10 ml of acid. The solution of salts was evaporated in vacuo at 30° to a volume of 50 ml and then acidified with 1 g of concentrated sulfuric acid. After 4 extractions with ether, followed by drying over sodium sulfate and removal of the solvent by distillation, we obtained 1.5 g of crystals with m.p. 70-80°. Recrystallization from petroleum ether gave 0.8 g of hydroxy acid with m.p. 106-109°, which did not depress the melting point when mixed with cis-2-methylcyclohexanol-1--carboxylic acid (VI). In addition, we obtained 0.55 g of crystals with m.p. 87-89°, which gave a melting point depression when mixed with the cis-hydroxy acid (VI) or with the trans-hydroxy acid (VII), and were the 2-methylcyclohexenecarboxylic acid [7,8,24].

b) A solution of 2.21 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) in 30 ml of acetone was added with stirring and water cooling to the moist silver oxide obtained from 4 g of silver nitrate. The mixture was stirred for 3 hours at 20° and then allowed to stand overnight. The next day the acetone was evaporated in vacuo, while the residue was diluted with 100 ml of water and then acidified with 100 ml of dilute hydrochloric acid. The product was extracted with ether in a Soxhlet apparatus for 20 hours and the ether extract dried over sodium sulfate. After removal of the ether by distillation we obtained 1.3 g of a crystallizing oil, from which by recrystallization from petroleum ether we isolated 0.7 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 109-110°. We isolated 0.5 g of an oil from the mother liquor, which could hot be made to crystallize.

Methyl ester of 1-bromo-2-methylcyclohexanecarboxylic acid. a) A dry ether solution of diazomethane (from 6 g of nitroso-methyl-urea) was added with cooling to an ether solution of 4.42 g of 1-bromo-2-methylcyclohexanecarboxylic acid (IX) and the mixture was allowed to stand for 2 hours at 20°. After removal of the ether by distillation, followed by fractional distillation on the product in vacuo, we obtained 3.7 g of the methyl ester of the bromo acid with b.p. 79-80° (3 mm), n_D^{19} 1.4942.

b) A mixture of 8.2 g of the bromide of trans-2-methylcyclohexanecarboxylic acid (VIII) and 7 g of bromine was heated on the water bath for 2 hours at 70° and for 3 hours at 100°, after which the mixture was poured with cooling into 4 volumes of anhydrous methyl alcohol, alowed to stand for 2 days, diluted with 100 ml of water, and extracted 4 times with ether. The ether extract was washed with water, then with sodium sulfite solution, dried over calcium chloride, the ether distilled off, and the product fractionally distilled in vacuo. We obtained 8.5 g of the methyl ester of the bromo acid with b.p. 76-78° (2.5 mm), n_D^{19} 1.4942.

Saponification of the methyl ester of 1-bromo-2-methylcyclohexanecarboxylic acid. A mixture of 11.75 g of the above described methyl ester of the bromo acid, 8 g of sodium hydroxide, 75 ml of water and 100 ml of methyl alcohol was stirred at 20° for 25 hours. Then the mixture was saturated with sodium chloride and extracted thoroughly with ether. We isolated 1 g of starting bromo acid methyl ester from the ether extract. Acidification of the alkaline solution, followed by extraction with ether, gave 5.1 g of a crystallizing oil, from which by recrystallization from petroleum ether we isolated 1.3 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) with m.p. 110-111°. The mother liquor was washed repeatedly with water (100 ml), dried over magnesium sulfate, and evaporated. We obtained 2.2 g of 2-methylcyclohexenecarboxylic acid as colorless crystals with m.p. 83-86° (from water). The water solution by extraction with ether in a Soxhlet apparatus gave 1.6 g of a crystallizing oil, from which by recrystallization from petroleum ether we obtained another 0.5 g of the cis-hydroxy acid (VI) with m.p. 901-110°. The methyl ester of the bromo acid could not be saponified with 2% aqueous sodium hydroxide solution at 20° for 18 hours.

Reduction of 1-bromo-2-methylcyclohexanecarboxylic acid (IX). A solution of 15.5 g of 1-bromo-2--methylcyclohexanecarboxylic acid in 100 ml of alcohol was treated under cooling with 13.2 g of activated zinc dust and the mixture allowed to stand overnight, after which it was refluxed for 6 hours. The zinc was filtered, washed with alcohol, the alcohol solution evaporated and residual oil washed with water, then with hydrochloric acid, and finally extracted with ether. Here an oil with a high bromine content was obtained, which was dissolved in 40 ml of glacial acetic acid, and then 13.2 g of activated zinc dust was added in portions at 5-8°. The mixture was allowed to stand overnight, after which it was heated for 1 hour on the boiling water bath. The product after cooling was extracted with ether and fractionally distilled in vacuo. Here we obtained 7.2 g of mixed stereoisomeric 2-methylcyclohexanecarboxylic acids with b.p. 105-106° (5 mm), n_D^{20} 1.4635, which when treated with thionyl chloride and then aniline gave 7.8 g of a mixture of anilides with m.p. 109-113°.

Found %: N 6.65, 6.85. $C_{14}H_{19}ON$. Calculated %: N 6.45.

Repeated fractional crystallization from benzene and aqueous methyl alcohol enabled us to isolate the anilide of cis-2-methylcyclohexanecarboxylic acid (X) with m.p. 124-126° and the anilide of trans-2-methylcyclohexanecarboxylic acid (VIII) with m.p. 149-151°, neither of which gave a melting point depression when mixed with the authentic specimens.

Methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid. An ether solution of diazomethane (from 12 g of nitroso-methyl-urea) was added to a solution of 15.8 g of cis-2-methylcyclohexanol-1-carboxylic acid (VI) in 100 ml of ether and the mixture allowed to stand for 2 hours at 20°. The product was washed with saturated sodium bicarbonate solution, dried over sodium sulfate, and vacuum-distilled. We obtained 10.8 g of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid with b.p. 66° (3 mm), n_D^{20} 1.4620.

Found %: C 62.48, 62.58; H 9.37, 9.46. $C_9H_{16}O_3$. Calculated %: C 62 74; H. 9.37.

Reduction of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid. A solution of 10.4 g of the methyl ester of cis-2-methylcyclohexanol-1-carboxylic acid in 50 ml of absolute ether was added with stirring to a solution of 4.5 g of aluminum lithium hydride in 300 ml of absolute ether. When exothermic reaction had ceased the mixture was refluxed on the water bath for 11 hours, then 15 ml of ethyl acetate was added, the mixture was acidified with dilute sulfuric acid until acid to litmus and then neutralized with solid sodium bicar-

bonate. The ether solution after drying and fractional distillation gave 8.3 g of cis-1-hydroxymethyl-2-methylcyclohexanol (XIII) with m.p. 64-65° (from petroleum ether).

Found %: C 66.58, 66.52; H 11.22, 11.08. $C_8H_{16}O_2$. Calculated %: C 66.67; H 11.11.

Preparation and reduction of monotosylate of cis-1-hydroxymethyl-2-methylcyclohexanol (XIV). A solution of 6.3 g of cis-1-hydroxymethyl-2-methylcyclohexanol (XIII) in 45 ml of absolute pyridine was cooled to 0° and then 10 g of toluenesulfonyl chloride was added in portions with stirring. The mixture was allowed to stand overnight at 0°, after which 100 ml of saturated sodium bicarbonate solution was added, the product extracted with ether, the ether extract washed with dilute sulfuric acid, then with saturated sodium bicarbonate solution, and dried over sodium sulfate. After distilling off the solvent in vacuo we obtained 14.5 g of the tosylate (XIV) as a brown oil, which could not be made to crystallize.

A solution of 16 g of the above described crude tosylate (XIV) in 70 ml of absolute ether and 70 ml of absolute benzene was added with stirring to a suspension of 6 g of aluminum lithium hydride in 150 ml of absolute ether and 150 ml of absolute benzene. The mixture was boiled under reflux for 20 hours, after which 30 ml of ethyl acetate was added, and the mixture first acidified with dilute sulfuric acid and then neutralized with solid sodium bicarbonate. After the usual treatment and fractional distillation in vacuo we obtained 5 g of cis-1,2-dimethylcyclohexanol (XI) with b.p. 73-75° (18 mm), n_D^{20} 1.4649, and m.p. 23.5-24° (from petroleum ether).

Found %: C 74.43, 74.54; H 12.46, 12.63. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

Literature [11]: b. p. 23.2°, b.p. 82-85° (25 mm), n_{5015}^{20} 1.4649.

Methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid. An ether solution of diazomethane (from 14 g of nitroso-methyl-urea) was added with cooling to an ether solution of 10.9 g of trans-2-methylcyclohexanol-1-carboxylic acid (VII) (m.p. 94-95°) and the mixture allowed to stand for 3 hours at 20°. After the usual treatment and fractional distillation in vacuo we obtained 11.3 g of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid with b.p. 56° (3 mm), n_D^{20} 1.4535.

Found %: C 62.75, 62.84; H 9.45, 9.35. $C_9H_{16}O_3$. Calculated %: C 62.74; H 9.37.

Reduction of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid. The reduction of 10.6 g of the methyl ester of trans-2-methylcyclohexanol-1-carboxylic acid with 4.5 g of aluminum lithium hydride was run in the same manner as described before, but the boiling time was increased to 23 hours. Fractional distillation in vacuo gave 8.3 g of trans-1-hydroxymethyl-2-methylcyclohexanol (XV) with b.p. 97° (3 mm), n_D^{20} 1.4890.

Found %: C 66.67, 66.48, H 10.90, 11.00. $C_8H_{16}O_2$. Calculated %: C 66.67; H 11.11.

Preparation and reduction of the monotosylate of trans-1-hydroxymethyl-2-methylcyclohexanol (XVI). Toluenesulfonyl chloride (13.5 g) was added in portions at 0° to a solution of 8.2 g of trans-1-hydroxymethyl-2-methylcyclohexanol (XV) in 40 ml of anhydrous pyridine. The mixture was allowed to stand at 0° for 2 days and then was worked up in the manner described above. We obtained 17.2 g of the tosylate (XVI) as a crystallizing oil. Recrystallization of a portion of the latter from a mixture of benzene and petroleum ether gave crystals with m.p. 60-61°.

Found %: C 60.51, 60.44; H 7.36, 7.36; S 10.70, 10.89. $C_{15}H_{22}O_4S$. Calculated %: C 60.37; H 7.44; S 10.73.

A solution of 16.6 g of crude tosylate (XVI) in 100 ml of absolute benzene was added to a suspension of 6.8 g of aluminum lithium hydride in 220 ml of absolute ether and 120 ml of absolute benzene, after which the mixture was refluxed for 23 hours and then decomposed with 45 ml of ethyl acetate. Here we obtained 4.4 g of trans-1,2-dimethylcyclohexanol (XII) with b.p. 71.5° (25 mm), n_D^{20} 1.4610, and m.p. 11-13°.

Found %: C 74.60, 74.40; H 12.48, 12.45. $C_8H_{16}O$. Calculated %: C 74.92; H 12.50.

Literature [11]: b.p. 13.2°, b.p. 74° (25 mm), n_{5015}^{20} 1.4614.

SUMMARY

The stereochemistry of the addition of hydrogen cyanide and of acetylene to 2-methylcyclohexanone was studied, and the configuration of the resulting 1-cyano-2-methylcyclohexanols, 1-ethynyl-2-methylcyclohexanols and their derivatives (hydroxy acids, ketols, keto diols, etc.) was established.

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INVESTIGATIONS IN THE FIELD OF POLYMETHYLENE RINGS

XXX. REACTION OF DIACETYL AND DIBENZOYL WITH DIMETHYLHYDRAZINE

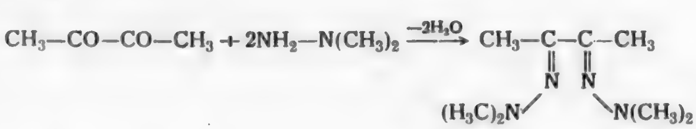
N. A. Domnin, V. I. Diurnbaum, and V. A. Cherkasova

It was shown by us that cyclopentanedione-1,2, cyclohexanediones-1,2 and -1,4 [1], and also pentanedione-2,4 (acetylacetone) [2], and hexanedione-2,5 (acetonylacetone) [3], readily give stable mono- and bis-dimethylhydrazones on reaction with dimethylhydrazine. In contrast to the enumerated diketones, cyclohexanedione-1,3 and 5,5-dimethylcyclohexanedione-1,3 (dimedon), and also dibenzoylmethane, reacting under the same conditions with dimethylhydrazine, give only monodimethylhydrazones and do not give bisdimethylhydrazones at all.

At the same time it was established by us that of all the dihydrazones obtained, the most unstable are those of cyclopentanedione-1,2 and cyclohexanedione-1,2. These facts were explained by us on the basis of the structure of the five- and six-membered rings and the steric hindrances resulting from the presence of $=N-NH_2$ and $=N-N(CH_3)_2$ groups in these cyclic dihydrazones.

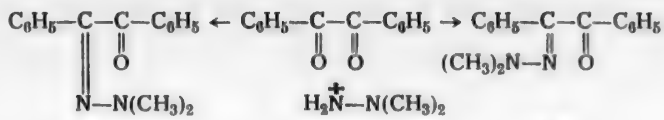
For further generalization of the facts obtained, however, it was necessary to carry out a comparative study of the reactions of the simplest aliphatic and aliphatic-aromatic 1,2-diketones with dimethyldrazine. For this purpose we also studied the reactions of diacetyl and dibenzoyl with dimethylhydrazine. With regard to this it should be noted that the reactions of diacetyl and dibenzoyl with hydrazine were studied by other investigators [4], while those with dimethylhydrazine have not been studied at all. Furthermore and to the point, as has been repeatedly shown, the reactions of the different diketones with hydrazine and dimethylhydrazine proceed quite differently, resulting in dissimilar products [1-3, 5].

The reaction of diacetyl with dimethylhydrazine takes place even at room temperature; however, a purer bisdimethylhydrazone was obtained after heating and stirring the mixture for 6 hours in a water bath at 60-70°. The reaction goes according to the scheme



Of the three possible geometric forms, the bisdimethylhydrazone is obtained only in one, the most probable anti-anti-form, in which two $N(CH_3)_2$ groups are directed toward opposite sides and lie at the maximum distance from one another.

The reaction of dibenzoyl (benzil) with dimethylhydrazine also takes place at room temperature; in this case crystals of the monodimethylhydrazone separate out from the solution within a day. However, the reaction goes more completely and more rapidly when the mixture is heated in a water bath at 80-90° for 2 hours. After removal of solvent, crystals of the monodimethylhydrazone are isolated, which after recrystallization from alcohol separate out in two forms, one the α- or syn-form (I), m.p. 99°, and the other the β- or anti-form (II), m.p. 86°. The reaction goes according to the scheme



(I) (II)

An x-ray diffraction investigation of the structures of the obtained geometric forms of the monodimethylhydrazone was conducted, which indicated the presence of polymorphism due to stereoisomerism.

The characteristics of the syn- and anti-form crystals are given in Table 2 in the experimental part.

However, only a complete study of diffraction densities can give an answer to the question of the structure of these geometric forms.

A spectrophotometric investigation of the stereoisomers (α- and β-forms) in the 3-12 μ infrared region was conducted with an IKS-11 spectrometer which had a NaCl prism. Clear absorption maxima were obtained in the 1650-1672 cm^{-1} region, corresponding to the valence vibrations of the carbonyl group in the β-form [9]. For the α-form in oil this wave number was faint (1642-1661 cm^{-1}), which was probably due to screening of the carbonyl group by methyl groups or by formation of a hydrogen bond between the carbonyl oxygen and a methyl hydrogen. Analysis of the rest of the spectrum shows that for the α- and β-forms, characteristic absorption maxima may be distinguished, which are exactly repeated for the given form, in spectra taken in oil and in CCl_4 solution. There are three regions for the α-form: 1053-1063, 923, and 874-875 cm^{-1}. There is one region for the β-form: 965-967 cm^{-1}.

In order to gain an understanding of the comparative characteristics of the spectra, the wave numbers for the most pronounced absorption maxima are listed in Table 1, the table being compiled in such a way that identical or similar numbers for different spectra lie on the same line.

We attempted to carry out the reaction of the monodimethylhydrazone with a second molecule of dimethylhydrazine to form the bisdimethylhydrazone, under various conditions, but without success. It turned out that the free carbonyl group of the benzil monodimethylhydrazone molecule reacts neither with dimethylhydrazine, nor with hydroxylamine, nor with hydrazine hydrate.

TABLE 1

Wave Numbers for the Most Pronounced Absorption Maxima in the Infrared Spectra *

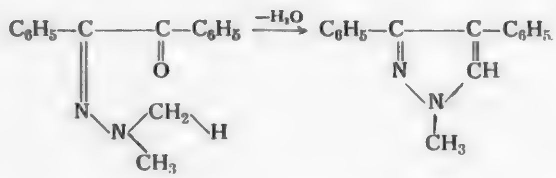
α-Form		β-Form		1-Methyl-3,4-diphenylpyrazole	Characteristics of vibrations for groups [9, 10]
in oil	in CCl_4, solution	in oil	in CCl_4 solution		
2959 (v.s.)	2890 (v.s.)	2890 (v.s.)	2907 (v.s.)		CH_3
1642 (w)	1661 (s.)	1651 (s.)	1672 (s.)		C=O
1567 (w.)	1558 (s.)	1558 (w.)	1558 (s.)		C=N
1456 (v.s.)	1445 (s.)	1453 (s.)	1453 (v.s.)	1464 (s.)	CH_3
1387 (s.)		1381 (s.)		1385 (s.)	—
1063 (s.)	1053 (s.)		1080 (w.)	1068 (s.)	CH_3
1016 (av.)	1020 (av.)	1020 (w.)	1022 (av.)	1020 (av.)	CH_3
.		965 (s.)	967 (s.)	955 (s.)	—
923 (s.)	923 (s.)	915 (av.)	917 (av.)	917 (av.	C—C
874 (s.)	875 (s.)				—
				852 (w.)	N—N
				825 (s.)	C—H

* The following abbreviations are used to denote the intensity of absorption: v.s. – very strong, s. – strong, av. – average, w. – weak.

On treatment of benzil monodimethylhydrazone with hydroxylamine under the conditions in which benzildioxime is formed [6], no reaction takes place and the monodimethylhydrazone is recovered unchanged. On treatment of benzil monodimethylhydrazone with hydrazine hydrate, benzil monohydrazone is obtained.

None of the attempts at synthesis of dibenzoyl bisdimethylhydrazone from dimethylhydrazine and benzil led to substitution of the second carbonyl group. As a result of a reaction carried out in alcoholic solution in sealed tubes which were heated for 5 hours at 100-110°, there was obtained a cyclization product of benzil monodimethylhydrazone – 1-methyl-3,4-diphenylpyrazole. The latter was also obtained simply by heating the crystalline monodimethylhydrazone in sealed tubes.

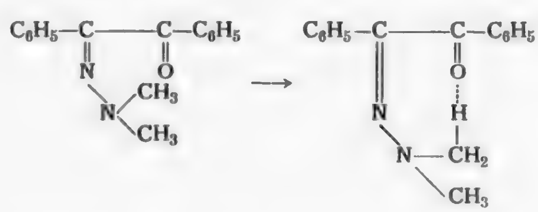
The formation of 1-methyl-3,4-diphenylpyrazole from benzil monodimethylhydrazone probably takes place according to the scheme



The experimental data obtained and the facts established give grounds for the assumption that the addition of 1 molecule of dimethylhydrazine to benzil to form the monodimethylhydrazone leads to a molecular structure in which the reaction of the second carbonyl group of the benzil with dimethylhydrazine is hindered. This may be explained more definitely by the fact that the two methyl groups bound to the nitrogen atom fill the space between the two phenyl groups quite closely, thus creating steric hindrances which make it impossible for dimethylhydrazine molecules to approach the remaining carbonyl group in the monodimethylhydrazone molecule. These steric hindrances may be interpreted as purely mechanical ones due to filling of the space, or they may be the result of the mutual influence of the atoms in the molecule, electron shifts, and effects which are for the present a matter of ideas and assumptions of a purely qualitative character. It will be possible to take up the description of these phenomena from the quantitative side only after the accumulation of more extensive factual and experimental material.

It was established earlier by us [1, 5] that cyclohexanedione-1,3 and dimedon, and also dibenzoylmethane, can form only monodimethylhydrazones, and are quite incapable of forming bisdimethylhydrazones. In all these cases we attempted to explain the inertness of the second carbonyl group in the molecules of the stated diketones by their capacity for enolization; however, we were unable to overcome the contradictions encountered in this problem.

One more possible hypothesis for explanation of the inertness of the carbonyl group in molecules of the monodimethylhydrazones of the diketones under discussion should be considered quite probable – this is the idea of the possibility of formation of a hydrogen bond between the carbonyl group and a hydrogen of a methyl group bound to a nitrogen atom, according to the scheme



In this case, of the two geometric forms of benzil monodimethylhydrazone, only the syn-form can give a hydrogen bond, while the anti-form must not be free to form a hydrogen bond.

This problem will be studied in continuing investigations of the hydrazones of cyclic diketones.

EXPERIMENTAL

It was necessary to dry the brown, technical dimethylhydrazine for several days over potassium hydroxide and to collect the fraction boiling from 55 to 56° in the first distillation. This clear fraction was dried again over potassium hydroxide and distilled, the fraction boiling from 62 to 64° being collected. This preliminary purification of the technical dimethylhydrazine, as we found out, is very important for its reaction with diketones and the purity of the products obtained.

Synthesis of diacetyl bisdimethylhydrazone. Into a three-neck, round-bottomed flask, provided with a mechanical stirrer, a reflux condenser, and a dropping funnel, was put 18 g (0.3 mole) of freahly distilled dimethylhydrazine (about 5-10% excess) in 20 ml of anhydrous ethyl alcohol. A solution of 8.6 g (0.1 mole) of diacetyl in 10 ml of anhydrous alcohol was introduced into the flask through a dropping funnel. The mixture was heated for 6 hours in a water bath at 60-70°. As a result there was obtained a clear, yellow solution, from which the alcohol was distilled at 50° and 200 mm pressure. The residue was fractionated in vacuo.

B.p. 70-72° (5 mm), d_4^{20} 0.9213, n_D^{20} 1.4940, MR_D 53.72; calculated 51.33.

Found %: C 56.78, 56.46; H 10.45, 10.39; N 33.28, 32.96, M 165.8, 163.3. $C_8H_{18}N_4$. Calculated %: C 56.47; H 10.58; N 33.28, M 170.

Synthesis of benzil monodimethylhydrazone. Benzoin and benzil were prepared according to Adams and Marvel [7] and Clark and Drepser [8]. After recrystallization from carbon tetrachloride, m.p. 93°; yield, 89%.

To a solution of 21 g (0.1 mole) of benzil in 63 ml of anhydrous alcohol was added 9 g (0.15 mole) of freshly distilled dimethylhydrazine. After heating in a water bath at 80-90° for 2 hours, the mixture was transferred to a Wurtz flask, and the bulk of the alcohol was distilled off in vacuo at 20-30°. The light-yellow precipitate thus formed had an indefinite melting point from 60-70° after drying. There was obtained 22 g (87 7%) of the substance. On recrystallization from alcohol there were obtained crystals of two forms, the larges and most characteristic crystals of which were mechanically withdrawn and studied separately.

α-Form. The clear, white crystals, twice recrystallized from anhydrous alcohol, had m.p. 99°. The substance was soluble in alcohol, ether, benzene, dioxane, and carbon tetrachloride and insoluble in water or alkalis either in the cold or on heating. On standing in air it was stable and did not change.

Found %: N 11.24, 11.25, M 235.3, 240.7. $C_{16}H_{16}ON_2$. Calculated %: N 11.11, M 252.

β-Form. Fine, bright-yellow crystals with m.p. 86°, having greater solubility than the α-form in the same solvents; like the α-form, they were insoluble in water and alkalis and stable on standing. The melting point, after two recrystallizations from anhydrous alcohol, was 86°.

Found %: N 11.32, 11.01. M 237.3, 244.6. $C_{16}H_{16}ON_2$. Calculated %: N 11.11, M 252.

On the basis of X-ray diffraction data the diffraction densities for the two stereoisomeric α- and β-forms of benzil monodimethylhydrazone were calculated. For comparative characteristics pycnometric densities (d_4^{20}) were experimentally determined: the value for the α-form was 1.199 and that for the β-form 1.156.

The X-ray diffraction data are given in Table 2.

Spectrophotometric investigation of the α- and β-forms of benzil monodimethylhydrazone in the infrared region. The first absorption spectrum was taken for the α-form (m.p. 99°) in vaseline oil: 17% of the oil, 0.02 mm layer. The data of interpretation are shown in Figure 1.

The second absorption spectrum for the α-from was taken in CCl_4 solution: 1% solution, 0.5 mm layer. The results of interpretation are shown in Figure 2.

The third absorption spectrum was taken for the β-form (m.p. 86°) in vaseline oil: 20% of the oil, 0.2 mm layer. Results are shown in Figure 3.

The fourth absorption spectrum was taken for the β-form in CCl_4 solution: 6% solution, 0.5 mm layer. Results are shown in Figure 4.

The absorption maxima in the infrared region of the spectrum for the α- and β-forms of benzil monodimethylhydrazone in oil and in CCl_4 solution are listed below.

TABLE 2

Characteristic		Yellow modification, β-anti-form	Colorless modification, α-syn-form
Melting point		86°	99°
Laue class		$\frac{2}{m}$	$\frac{2}{m}$
Syngony		Monoclinic	Monoclinic
Diffraction group		$3; \frac{2}{m} P \frac{2_1}{-} \boxed{\kappa}$	$3; \frac{2}{m} P \frac{2_1}{-} \boxed{\kappa}$
Space group		$P \frac{2_1}{m}$ or $P2_1$	$P \frac{2_1}{m}$ or $P2_1$
Unit-cell dimensions	a	11.48 kX	8.12 kX
	b	8.47 kX	15.13 kX
	c	14.30 kX	11.34 kX
	β	90°	78°35′
Pycnometric density		1.156 g/cm^3	1.199 g/cm^3
X-ray diffraction density		1.172 g/cm^3	1.195 g/cm^3
Unit-cell volume		1420 kX^3	1380 kX^3
Number of molecules [formula units] per unit cell		4 (3.95)	4 (3.95)

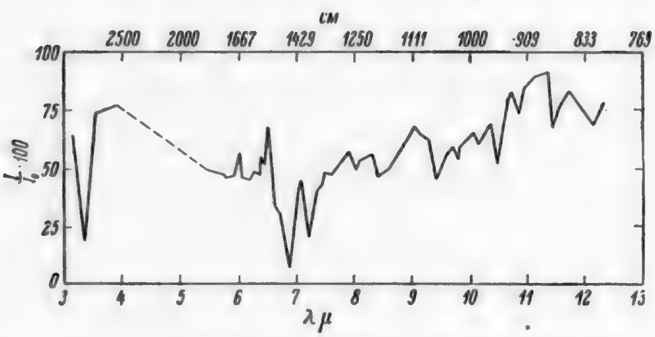


Fig. 1. Transmission curve of the α-form of benzil monodimethylhydrazone in oil.

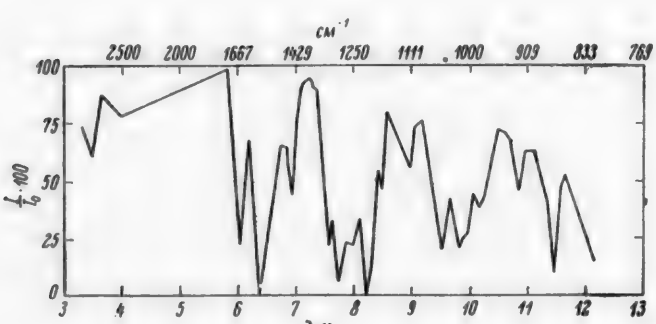


Fig. 2. Transmission curve of the α-form of benzil monodimethylhydrazone in CCl_4 solution.

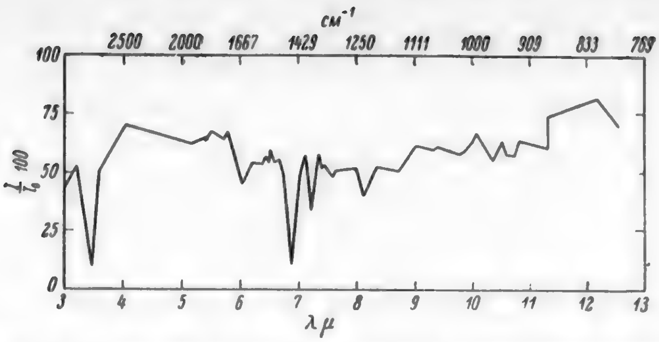


Fig. 3. Transmission curve of the β-form of benzil monodimethylhydrazone in oil.

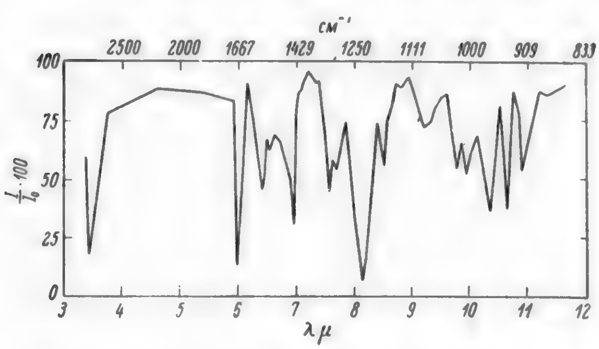


Fig. 4. Transmission curve of the β-form of benzil monodimethylhydrazone in CCl_4 solution.

α-Form in oil: 3.38 (v. s.), 5.92 (av.), 6.09 (w.), 6.38 (w.), 6.87 (v. s.), 7.22 (s.), 7.59 (w.), 8.04 (av.), 8.40 (w.), 9.42 (s.), 9.84 (av.), 10.24 (s.), 11.44 (s.).

α-Form in CCl_4 solution: 3.46 (v. s.), 6.02 (s.), 6.42 (s.), 6.92 (s.), 7.55 (w.), 7.72 (w.), 8.47 (w.), 9 50 (s.), 9.80 (s.), 10.84 (s.), 11.43 (s.).

β-Form in oil: 3.46 (v. s.), 6.06 (s.), 6.42 (w.), 6.58 (av.), 6.88 (s.), 7.24 (s.), 7.60 (w.), 8.16 (av.), 9.80 (w.), 10.36 (s.), 10.71 (av.), 10.92 (av.).

β-Form in CCl_4 solution: 3.44 (v. s.), 5.98 (s.), 6.42 (s.), 6.54 (av.), 6.88 (v. s.), 7.55 (av.), 7.68 (w.), 8.16 (av.), 8.52 (s.), 9.26 (w.), 9.78 (av.), 9.94 (av.), 10.34 (s.), 10.64 (s.), 10.90 (av.).

Decomposition of benzil monodimethylhydrazone. To 2.5 g of benzil monodimethylhydrazone (unrecrystallized product) was added 30 ml of 10% hydrochloric acid. The substance dissolved after a while, and on standing, a white, acicular precipitate (about 2 g) formed, which, after recrystallization from anhydrous alcohol, had m.p. 96°. A test combustion revealed the absence of nitrogen in the substance. A mixture test with known benzil gave no depression.

Action of hydrazine hydrate on benzil monodimethylhydrazone. To 2.5 g (0.1 mole) of benzil monodimethylhydrazone in 12 ml of anhydrous alcohol was added 0.75 g (0.15 mole) of hydrazine hydrate in 3 ml of alcohol. The mixture was boiled in a water bath for 5 hours. From the cooled solution, 1.85 g of a white, crystalline precipitate separated out. After recrystallization from alcohol the substance had m.p. 150-151°. A mixture test with known benzil monohydrazone showed no depression.

Conversion of benzil monodimethylhydrazone to 1-methyl-3,4-diphenylpyrazole. To 7 g of benzil in 21 ml of anhydrous alcohol was added 5 g of dimethylhydrazine. The mixture was heated in a water bath for

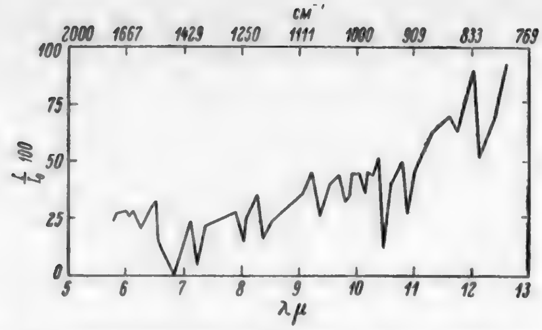


Fig. 5. Transmission curve of 1-methyl-3,4-diphenyl- pyrazole in oil.

10 hours at 85-90° and left overnight. On recrystallization of the precipitate formed, only benzil monodimethylhydrazone was found. For the purpose of seeking the conditions for the synthesis of benzil bisdimethylhydrazone, the reaction of benzil with dimethylhydrazine was carried out in sealed tubes. Five g of benzil, 10 ml of anhydrous alcohol, and 3 g of dimethylhydrazine were sealed into the tube, which was heated in an oven at 100-110° for 5 hours. After 2 days the tube was opened, and 2 g of a crystalline substance which was recrystallized and had m.p. 160°, was isolated from the reaction mixture by suction filtration. The alcohol was distilled off from the filtrate; in the residue a yellow oil of unknown structure, which did not distill in vacuo, was obtained. Carrying out the experiment under the same conditions of heating in a tube for 5 hours, but at 120-130°, leads mainly to the same product with m.p. 160° and a small amount of a new substance with m.p. 114-115°.

On heating 10 g of benzil with 6 g of dimethylhydrazine in a sealed tube for 10 hours at 150-160°, three distinct substances were isolated from the reaction products. Recrystallized from alcohol, they had m. p. 160° (about 3 g), 114°, and 232° (small amounts).

Substance with m.p. 160°. Found %: C 81.93, 81.78; H 6.19, 6.04, N 11.94, 12.09. M 219.8, 221.5. $C_{16}H_{14}N_2$. Calculated %: C 82.05; H 5.98; N 11.96, M 234.

On the basis of analyses, molecular weight, and the results of a spectrophotometric study of the infrared spectra of the substance obtained, the structure of 1-methyl-3,4-diphenylpyrazole should be assigned to it.

With NaCl prism, the 3-12 μ region was taken in vaseline oil: 33% paste, 0.04 mm layer. Results are shown in Figure 5. The following absorption maxima were found in the infrared region of the spectrum for 1--methyl-3,4-diphenylpyrazole in oil: 6.83 (s.), 7.22 (s.), 8.05 (w.), 8.38 (w.), 9.36 (s.), 9.80 (av.), 10.14 (av.), 10.47 (s.), 10.90 (av.), 11.74 (w.), 12.12 (s.).

Substance with m.p. 114°. Found %: C 83.68, 83.78; H 5.35, 5.26; N 5.00, 5.06. $C_{20}H_{15}ON$. Calculated %: C 83.79; H 4.93; N 4.93.

The structure of this substance remained unknown; it was not possible to determine even its molecular weight.

Substance with m.p. 232°. Found %: C 78.60, 78.37; H 6.46, 6.50; N 4.70, 4.57. $C_{20}H_{20}ON_2$. Calculated %: C 78.43; H 6.53; N 4.57.

The molecular weight could not be determined; the structure of the substance remained unknown.

Into one of the tubes of a Terent'ev reactor was put 2 g of the monodimethylhydrazone, and into the other was put 2 g of anhydrous cupric sulfate. After heating for one-half hour in an oil bath at 120-130°, the monodimethylhydrazone became distended, and crystals separated out from the molten mass. After recrystallization from alcohol there was obtained 1.45 g (73%) of a clear, crystalline product with m.p. 160°, which proved to be 1-methyl-3,4-diphenylpyrazole and which was readily soluble in alcohol, benzene, and ether and insoluble in cold and hot water and in alkalis. When it was added to 10% hydrochloric acid, it dissolved rapidly and spontaneously. Alkalinization of the solution caused formation of a white, flocculent precipitate which, after washing with water and alcohol, had m.p. 160°.

In conclusion we consider it a pleasant duty to express our sincere thanks to E. V. Stroganov for the X-ray structural investigation and to D. N. Glebovskii for recording the infrared spectra of the compounds obtained by us.

SUMMARY

1. Diacetyl bisdimethylhydrazone has been obtained and characterized for the first time.

2. It has been established that dibenzoyl (benzil) reacts with only one molecule of dimethylhydrazine and thereby gives two steric α- and β-forms of the monodimethylhydrazone. Both of these forms have been characterized.

3. It has been established that benzil does not form bisdimethylhydrazones and that the carbonyl group of the monodimethylhydrazone reacts neither with hydroxylamine, nor with hydrazine, nor with dimethylhydrazine.

4. It has been established that when benzil monodimethylhydrazone reacts with hydrazine hydrate, benzil hydrazone is obtained.

5. It has been established that on heating, benzil monodimethylhydrazone cyclizes to 1-methyl-3,4-diphenylpyrazole.

6. The facts obtained are explained in the light of the steric structures of the mono- and bisdimethylhydrazone molecules and the steric hindrances which arise in these molecules.

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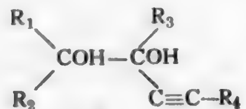
**In Russian.

INVESTIGATION OF TRANSFORMATIONS OF PINACOLS WITH SUBSTITUTED ACETYLENIC RADICALS

XVI. SYNTHESIS AND TRANSFORMATIONS OF SYM. DIMETHYLPHENYL(TERT-BUTYLETHYNYL)ETHYLENE GLYCOL (3,6,6-TRIMETHYL-2-PHENYL-HEPTYN-4-DIOL-2,3)

E. D. Venus-Danilova and V. I. Serkova

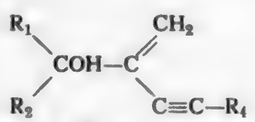
The study of the transformations of ditertiary α-glycols (pinacols) of the acetylene series (I) on catalytic treatment with sulfuric acid [1-3] showed that this transformation depends on the nature of the radicals R_1, R_2, R_3, and R_4 and on their disposition relative to each other in the glycol molecule.



(I)

Up to the present time 11 glycols of this type, containing methyl and aryl radicals (R_1, R_2, and R_3) attached to the hydroxylated carbon atoms 1 and 2 and a phenyl or tert-butyl (R_4) in the acetylenic radical, have been studied.

On heating with 20-46% sulfuric acid these glycols are transformed in three directions: 1) dehydration with formation of an enynic alcohol (II) [3] or decomposition products thereof [4]; 2) pinacoline rearrangement, as a result of which a ketone of the acetylene series (III) is obtained [5-9];. 3) isomerization of the glycol by a rearrangement of the acetylene-allene type with formation of an ethylenic γ- keto alcohol(IV) [10], for which further transformations are possible – formation of a dienic ketone (V) [11, 7], formation of products of the ketonic cleavage of the γ-keto alcohol (VI) [6, 8, 9], and cyclization of the γ-keto alcohol to form a substituted 2-hydroxy-dihydrofuran-2,5 (VII) [12, 10, 13,6].



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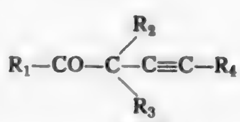

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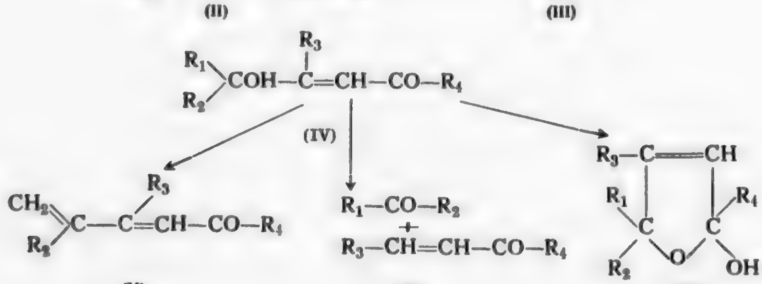
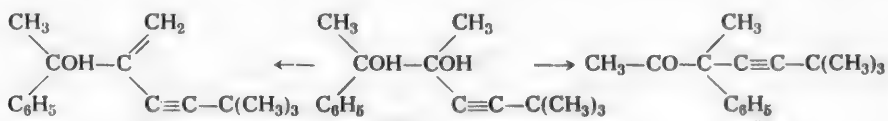


(IV) (V) (VI) (VII)

Any one transformation of acetylenic pinacols on treatment with sulfuric acid, for instance, the formation only of an acetylenic ketone [5], dehydration only [3, 4], or the formation only of a substituted hydroxydihydrofuran [13], was observed quite rarely. Usually the reaction goes in two or three directions with formation of various substances, but with one of them predominating.

It is noted that the dehydration of α-glycols (I) takes place in the presence of a methyl group on the second hydroxylated carbon atom ($R_3 = CH_3$) [3, 4], and the pinacoline rearrangement is facilitated by the presence of one or two phenyls on the first hydroxylated carbon atom ($R_1 = C_6H_5$ or $R_1 = R_2 = C_6H_5$) [5-7]. The isomerization of the glycol to an unsaturated γ-keto alcohol or products of the further transformation of the latter was observed to a greater or lesser degree with all the ditertiary α-glycols of the acetylene series, in the molecules of which there was an aryl radical on the second hydroxylated carbon atom (R_3 = aryl), regardless of the nature of the remaining radicals [6-10, 12, 13].

At present it is still impossible to predict accurately the direction of the transformations of pinacols of the acetylene series, since every radical occupying a definite position in the pinacol molecule influences its transformation. We observe only the total effect of these influences. However, the results obtained by us in the study of the transformations of sym. dimethylphenyl(phenylethynyl)ethylene glycol [4], unsym. methyldiphenyl-(tert-butylethynyl)ethylene glycol [3], unsym. methyldiphenyl(phenylethynyl)ethylene glycol [5], and trimethyl-(phenylethynyl)ethylene glycol [8], of which the first two gave only enynic alcohols and the last two gave ketones of the acetylene series, make a certain degree of foresight possible. It may be expected that on treatment with sulfuric acid sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (VIII) will be transformed either into an enynic alcohol (IX) or into a ketone of the acetylene series (X).

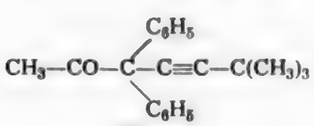


(IX) (VIII) (X)

In order to test this hypothesis we synthesized sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (VIII) and studied its transformation on heating with 30% sulfuric acid.

Methylphenylacetylcarbinol and tert-butylacetylene were used for the preparation of the glycol by the method of Zh. I. Iotsich. The structure of the glycol was confirmed by oxidation with lead tetraacetate [14].

The only product of transformation of this glycol under the influence of sulfuric acid proved to be a ketone of the acetylene series – unsym. methylphenyl-(tert-butylethynyl) acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2 (X), which readily formed a semicarbazone and a 2,4-dinitrophenylhydrazone. The structure of the ketone was proved by oxidation, by its infrared spectrum, and by comparison of its ultraviolet spectrum with the corresponding spectrum of unsym. diphenyl-(tert-butylethynyl)acetone (XI)* (Figure 1).



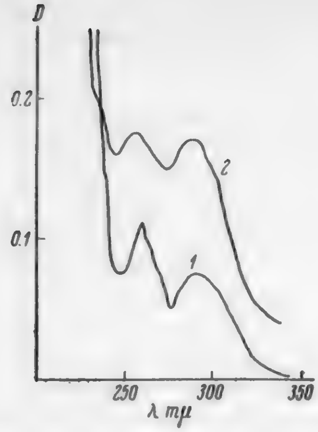
(XI)

EXPERIMENTAL

Sym. Dimethylphenyl-(tert-butylethynyl)ethylene Glycol (3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3) (VIII).

Synthesis of the glycol. To an ethereal solution of ethylmagnesium bromide, prepared in the usual way was added an ethereal solution of tert-butylacetylene (b.p. 38-39.5°) taken in 50% excess. Toward the end of

* This ketone was given to us by L. A. Pavlova, for which we express to her our thanks.



Ultraviolet spectra. 1) Unsym. methylphenyl-(tert-butylethynyl)acetone (X); 2) unsym. diphenyl-(tert-butylethynyl) acetone (XI).

the reaction, the reaction mass was warmed (water-bath temperature 38-40°) until the evolution of ethane was complete. Methylphenylacetylcarbinol (b.p. 122-123° at 8 mm) dissolved in absolute ether, was slowly added to the organomagnesium compound of tert-butylacetylene, the latter being cooled with ice, and vigorously stirred.. After three days the organomagnesium complex was decomposed, and the reaction product was extracted with ether and dried with sodium sulfate. After the ether was distilled off, the residual mass quickly crystallized. By recrystallization from petroleum ether there was isolated a finely crystalline, colorless substance with m.p. 84-85°, which gave a positive reaction for the hydroxyl group (with methylmagnesium iodide), and also decolorized an aqueous solution of potassium permanganate and a solution of bromine in chloroform.

The average yield of the glycol from three experiments amounted to 70%, calculated on the basis of the methylphenylacetylcarbinol taken.

Found %: C 77.94, 77.88; H 9.16, 8.98. Number of hydroxyl groups 2.1. M 247. $C_{16}H_{22}O_2$. Calculated %: C 78.04; H 8.94. Number of hydroxyl groups 2. M 246.

On the basis of the analytical data and properties, the substance with m.p. 84-85° should be regarded as 3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3.

Oxidation of the glycol. To 5 g of the acetylenic glycol, dissolved in 50 ml of glacial acetic acid, was added in small portions 11 g of lead tetraacetate (20% excess) with vigorous stirring [14]. The mixture was heated for 3 hours, the acetic acid was half neutralized with aqueous potash solution, and the reaction products were steam distilled. Three fractions of the distillate were taken; from each one separately an ether extract was made which was washed with potash solution until a neutral reaction was obtained and dried with sodium sulfate. After the ether was distilled off from all three fractions, liquid products were obtained which gave a qualitative reaction for the carbonyl group. The material of the first fraction – a light-yellow liquid – formed a precipitate with 2,4-dinitrophenylhydrazine, which was not fully soluble in boiling ethyl alcohol. The boiling alcoholic solution was cooled, and from it light-yellow crystals with m.p. 164° were isolated, which gave no melting-point depression with known methyl tert-butylethynyl ketone 2,4-dinitrophenylhydrazone.

Found %: C 55.04; H 5.48; N 17.73. $C_{14}H_{16}O_4H_4$. Calculated %: C 55.26; H 5.26; N 18.41.

The infrared spectrum of the material of the first fraction indicates that there are a triple bond and a carbonyl group in the molecule of this substance, which fact also confirms the presence of methyl tert-butylethynyl ketone.

The residue insoluble in boiling ethyl alcohol on recrystallization of methyl tert-butylethynyl ketone 2, 4-dinitrophenylhydrazone (m.p. 164°) was dissolved in glacial acetic acid on heating. In this case there were obtained red crystals with m.p. 248°. A mixture test with known acetophenone 2,4-dinitrophenylhydrazone (m.p. 249°) showed no melting-point depression. The semicarbazone with m.p. 198° also corresponded to acetophenone.

Thus the oxidation products of the acetylenic glycol (acetophenone and methyl tert-butylethynyl ketone) confirmed the hypothesis that the acetylenic glycol has the structure of sym. dimethylphenyl-(tert-butylethynyl) ethylene glycol.

Unsym. Methylphenyl-(tert-butylethynyl)acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2) (X).

Action of 30% sulfuric acid on sym.dimethylphenyl-(tert-butylethynyl)ethylene glycol. Seven g of the glycol (mp. 84-85°) was gently boiled with a 10-fold quantity of sulfuric acid for 3 hours. The glycol melted, and the liquid gradually assumed a greenish-yellow hue, but neither resin formation nor fluorescence was observed. The ether extract from the acid solution was washed with dilute aqueous soda solution and dried with

sodium sulfate. No products were isolated from the ether extract of the neutralized solution.

After the ether was eliminated from the extract of the acid solution, the light-yellow liquid obtained gave no reaction for the hydroxyl group, decolorized a solution of bromine in chloroform and aqueous potassium permanganate solution, and reacted with 2,4-dinitrophenylhydrazine and a solution of semicarbazide.

B.p. 100-101° (3 mm), d_{20}^{20} 0.9258, d_4^{20} 0.9242, n_D^{20} 1.4993, MR_D 72.47. $C_{16}H_{20}OF_3F$. . Calculated 70.49.

Found %: C 84.27, 84.04; H 8.85, 8.88. M 227. $C_{16}H_{20}O$. Calculated %: C 84.21; H 8.77. M 228.

The yellow 2,4-dinitrophenylhydrazone was obtained under the usual conditions [15]. M. p. 121° (from alcohol).

Found %: C 64.80, 64.60; H 5.98, 6.01; N 13.56, 13.43. $C_{22}H_{24}O_4N_4$. Calculated %: C 71.57; H 8.08; N 14.73.

After recrystallization (from alcohol) the semicarbazone melted at 214°.

Found %: C 71.58, 71.68; H 7.94; N 15.03, 14.81. $C_{17}H_{23}ON_3$. Calculated %: C 71.57; H 8.08; N 14.73.

Oxidation of the ketone (b.p. 100-101° at 3 mm). For 3 g of the ketone, 6.9 g of potassium permanganate was taken (calculated on the basis of 5 atoms of oxygen per ketone molecule). To a solution of the ketone in 25 ml of pyridine, 250 ml of 2% aqueous potassium permanganate solution was added at once. The oxidation was carried out with vigorous agitation at room temperature. After the solution was decolorized, the remaining 1.9 g of oxidizing agent was added in small portions until decolorization of the solution ceased. The oxidation continued for 7 hours. When the oxidation was finished, the manganese dioxide was filtered out from the clear solution, washed 3 times with small portions of hot water and treated with ether. After removal of ether there remained about 0.3 g of the original ketone, which was characterized by the 2,4-dinitrophenylhydrazone, b.p. 120°.

The pyridine and neutral oxidation products volatile with steam were distilled off from the filtrate at a low rate on heating. In the distillation the pyridine was converted to the salt by the calculated quantity of dilute sulfuric acid, after which an ether extract was made; from the latter there was isolated acetophenone, characterized by the semicarbazone (m.p. 198°) and the 2,4-dinitrophenylhydrazone (m.p. 247°) (mixture tests). Neutral oxidation products not volatile with steam were not found.

After the salts of the organic acids were concentrated and cautiously composed with dilute sulfuric acid, an oily substance was isolated from them, which was extracted with ether. After evaporation of the ether, water was added to the oily residue and the mixture was boiled; the volatile organic acids were then separated by steam distillation. From the three distillates obtained, stable silver salts were isolated by boiling with freshly precipitated silver carbonate. The silver content in these salts was determined after fractional recrystallization.

Found I distillate, 1st fraction %: Ag 51.81; I distillate, 3rd fraction %: Ag 53.91; III distillate, 1st fraction %: Ag 62.05, III distillate, 2nd fraction %: Ag 64.42. CH_3COOAg. Calculated %: Ag 64.65. $(CH_3)_3COOAg$; %: Ag 51.67.

After the acids volatile with steam were distilled off, there was extracted with ether a very insignificant quantity of a very impure solid substance with a sharply acid reaction, which vigorously decolorized aqueous potassium permanganate solution, and which was not further investigated.

The formation of acetophenone, acetic acid, and trimethylacetic acid on oxidation of ketone (X) (b.p. 100-101° at 3 mm) confirms the formula proposed for the ketone.

When a smaller amount of the oxidizing agent was used (4 atoms of oxygen per ketone molecule), trimethylpyruvic acid was also found among the acid products; it was isolated from the acid mixture in the form of the rapidly precipitated, yellow 2,4-dinitrophenylhydrazone, m.p. 174° after recrystallization from alcohol. A mixture test with the 2,4-dinitrophenylhydrazone (m.p. 174°) obtained from specially synthesized trimethylpyruvic acid [16] showed no melting-point depression.

Found %: C 46.14; H 4.48; N 18.20, 18.30. $C_{12}H_{14}O_6N_4$. Calculated %: C 46.16; H 4.49; N 18.06.

Spectra of unsym. methylphenyl-(tert-butylethynyl)acetone (X). The ultraviolet spectrum was taken in ethyl alcohol with an SF-4 spectrophotometer. For comparison the spectrum of unsym. diphenyl-(tert-butylethynyl)acetone (X) was also obtained under similar conditions. The obvious similarity of the absorption curves for the two ketones may be seen in the figure. The maxima and minima correspond to the same wavelengths: (X) – λ_{max} 260 mμ ϵ 560; λ_{max} 296 mμ, ϵ 375. (XI) – λ_{max} 258 mμ, ϵ 890; λ_{max} 290 mμ, ϵ 870.

The infrared spectrum of unsym. methylphenyl- (tert-butylethynyl)-acetone (X) was taken with an IKS-12 single-beam spectrometer provided with LiF and NaCl prisms, as well as an F-1 glass prism. The spectrum showed that ketone (X) contains an unconjugated carbonyl group (1724 cm^{-1}) and an acetylenic bond (2224 cm^{-1}). Bands of the monosubstituted benzene nucleus (1600, 1498, 705 cm^{-1}) and apparently the $(CH_3)_3C-$ group (1277 cm^{-1}) are also present in the spectrum. The characteristic frequencies of the CH_2 group – 6100 and 810 cm^{-1} – are absent in the spectrum.

The infrared spectra were taken by T. V. Iakovleva and the analyses were carried out by I. A. Maretina, for which we express to them our thanks.

SUMMARY

1. Sym. dimethylphenyl-(tert-butylethynyl)ethylene glycol (3,6,6-trimethyl-2-phenylheptyn-4-diol-2,3), not described in the literature, has been synthesized.

2. It has been shown that on heating with 30% sulfuric acid the glycol is converted to a ketone of the acetylene series – unsym. methylphenyl-(tert-butylethynyl)acetone (3,6,6-trimethyl-3-phenylheptyn-4-one-2).

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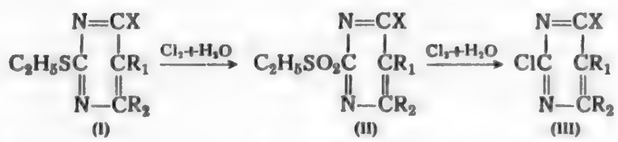
INVESTIGATIONS IN THE PYRIMIDINE SERIES. ACTION OF HYDROGEN PEROXIDE ON MERCAPTOPYRIMIDINES. FORMATION OF PYRIMIDINE SULFONES AND THEIR INSTABILITY IN THE PRESENCE OF HYDROGEN PEROXIDE

Ch'ih Yueh-fon and Ch'en Shu-feng

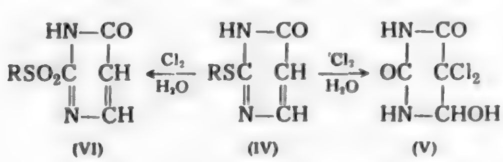
It is known that 2-ethylthiopyrimidines (I, X = Cl, OR, or NH_2), on reaction with chlorine in an aqueous medium at 0°, form pyrimidine sulfones (II, X = Cl, OR, or NH_2), which can easily be isolated [1-5].

This reaction follows a peculiar course: on treatment with chlorine the unsaturation of the pyrimidine ring (I) is unchanged, while the alkylthio group is oxidized, as a result of which a stable alkanesulfonylpyrimidine (II) is formed.

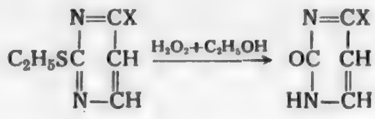


$R_1 = R_2 = H$; $R_1 = Br$, $R_2 = H$; $R_1 = C_2H_5$, $R_2 = CH_3$; $R_1 = CH_3$, $R_2 = H$; $R_1 = COOC_2H_5$, $R_2 = H$; $R_1 = R_2 = CH_3$; $R_1 = C_3H_7$-n, $R_2 = CH_3$.

Treatment with chlorine at a somewhat elevated temperature may lead to replacement of the ethanesulfonyl group of pyrimidine (II) by chlorine [1] with formation of a pyrimidine derivative (III). Thus 2-ethylthio-4-chloro-5-carboethoxypyrimidine (I, $R_1 = COOC_2H_5$, R_2 = H, X = Cl), on treatment with chlorine at 30-40°, was converted to 2,4-dichloro-5-carboethoxypyrimidine [1] (III, $R_1 = COOC_2H_5$, R_2 = H, X = Cl). At the beginning of the reaction, in this case, there was formed 2-ethanesulfonyl-4-chloro-5-carboethoxypyrimidine (II, $R_1 = COOC_2H_5$, R_2 = H, X = Cl), which by the further action of chlorine was converted to 2,4-dichloro-5-carboethoxypyrimidine (III, $R_1 = COOC_2H_5$, R_2 = H, X = Cl). Another case of replacement of the ethanesulfonyl group by chlorine was noted by Ch'ih and Ling. They found that 2-ethylthio-4-methoxy-5,6-dimethylpyrimidine (I, $R_1 = R_2 = CH_3$, X = OCH_3) on treatment with chlorine (at 0-15° in 90% aqueous methanol) gave 2-chloro-4-methoxy-5,6-dimethylpyrimidine (III, $R_1 = R_2 = CH_3$, X = OCH_3) and 2-ethanesulfonyl-5,6-dimethyl-4-methoxypyrimidine (II, $R_1 = R_2 = CH_3$, X = OCH_3) [4]. Johnson and Sprague [6] stated that 2-alkylthio-4-hydroxypyrimidines (IV) on treatment with chlorine water formed derivatives of 2,4-diketohexahydropyrimidine (V); 2-alkanesulfonyl-4-hydroxypyrimidines (VI) were not isolated in this case. This reaction may be represented in the following manner:

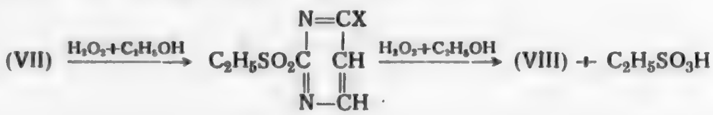


Ch'ih and Ch'en [7] found that on treatment of 2-ethylthiopyrimidines [VII, X = Cl OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] with hydrogen peroxide in ethanol, 2-hydroxypyrimidines [VIII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] are formed, as shown in the scheme



(VII) (VIII)

The authors proposed the following reaction mechanism:



(IX) (X)

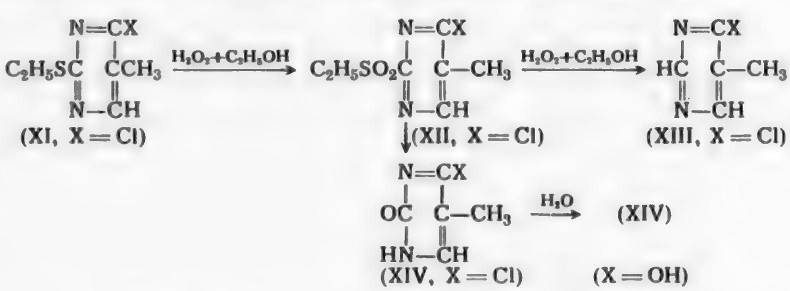
The proposed mechanism was experimentally supported by the fact that 2-ethanesulfonyl-4-chloropyrimidine [1] (IX, X = Cl), obtained by treatment of 2-ethylthio-4-chloropyrimidine with chlorine in water at 0°, reacts with hydrogen peroxide in ethyl alcohol to form 2-hydroxy-4-chloropyrimidine [7] (VIII, X = Cl). Ch'ih and Ch'en noted also that 2-ethylthio-4-alkoxypyrimidines (VII, X = OCH_3 or OC_2H_5) on reaction with hydrogen peroxide formed not only 2-hydroxy-4-alkoxypyrimidines (VIII, X = OCH_3 or OC_2H_5), but also uracil (VIII, X = = OH) [7]. The authors explained the formation of uracil as the result of the hydrolysis of 2-hydroxy-4-alkoxypyrimidines with the participation of ethanesulfonic acid (X) as catalyst:

$$\underset{(X = OCH_3 \text{ or } OC_2H_5)}{(VII)} \xrightarrow{H_2O_2 + C_2H_5OH} \underset{(X = OCH_3 \text{ or } OC_2H_5)}{(VIII) + (X)}$$

$$\underset{(X = OCH_3 \text{ or } OC_2H_5)}{(VIII)} \xrightarrow[H_2O]{C_2H_5SO_3H} \underset{(X = OH)}{(VIII)}$$

In the present article the action of hydrogen peroxide on 2-ethylthio-5-methylpyrimidines [XI, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] under various conditions is described in detail.

In the reaction of 2-ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl) with 30% hydrogen peroxide in ethyl alcohol, 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl), 4-chloro-5-methylpyrimidine (XIII, X = Cl), and thymine (XIV, X = OH) were formed. 4-Chloro-5-methylpyrimidine, the formation of which was rather unexpected, may have been obtained from 2-ethanesulfonyl-4-chloro-5-methylpyrimidine reduction with hydrogen peroxide. The isolation of thymine may serve to confirm the hypothesis that 2-hydroxy-4-chloro--5-methylpyrimidine (XIV, X = Cl) occurs in the reaction products and is converted to thymine on recrystallization from dilute ethyl alcohol or water. The given conversions are shown below.



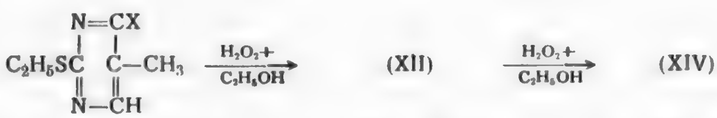
On treatment of a 2-ethylthio-4-alkoxy-5-methylpyrimidine (XI, X = OCH_3 or OC_2H_5) with 30% hydrogen peroxide in ethyl alcohol, there were obtained a 2-ethanesulfonyl-4-alkoxy-5-methylpyrimidine (XII, X = OCH_3

or OC_2H_5), a 2-hydroxy-4-alkoxy-5-methylpyrimidine, (XIV, X = OCH_3 or OC_2H_5), and thymine (XIV, X = OH). Apparently the pyrimidine sulfone, formed at the beginning of the reaction, reacted further with hydrogen peroxide to form a 2-hydroxy-4-alkoxy-5-methylpyrimidine (XIV, X = OCH_3 or OC_2H_5), which then was converted to thymine (XIV, X = OH) by the catalytic effect of ethanesulfonic acid also formed in the reaction. The scheme given below indicates the course of this reaction.

$$\underset{(X=OCH_3\ \text{or}\ OC_2H_5)}{(XI)} \xrightarrow{H_2O_2+C_2H_5OH} \underset{(X=OCH_3\ \text{or}\ OC_2H_5)}{(XII)} \xrightarrow{H_2O_2+C_2H_5OH} \underset{(X=OCH_3\ \text{or}\ OC_2H_5)}{(XIV)} + (X)$$

$$\underset{(X=OCH_3\ \text{or}\ OC_2H_5)}{(XIV)} \xrightarrow[H_2O]{C_2H_5SO_3H} \underset{(X=OH)}{(XIV)}$$

2-Ethylthio-4-amino-5-methylpyrimidine and its alkylamino derivatives [XI, X = NH_2, $NHCH_3$, or $N(C_2H_5)_2$] reacted with 30% hydrogen peroxide in ethyl alcohol to form 2-ethanesulfonyl-4-amino-5-methylpyrimidine and its alkylamino derivatives [XII, X = NH_2, $NHCH_3$, $N(C_2H_5)_2$], and 2-hydroxy-4-amino-5-methylpyrimidine and its alkylamino derivatives [XIV, X = NH_2, $NHCH_3$, or $N(C_2H_5)_2$]. The 2-ethanesulfonyl group in amino- and alkylaminopyrimidine sulfones [XII, X = NH_2, $NHCH_3$, or $N(C_2H_5)_2$] on treatment with hydrogen peroxide was easily replaced by a hydroxy group, whereupon 2-hydroxy-4-amino-5-methylpyrimidine or N-alkylaminopyrimidines [XIV, X = NH_2, $NHCH_3$, or $N(C_2H_5)_2$] were formed. These conversions are indicated by by the scheme



(XI), (X = NH_2, $NHCH_3$ or $N(C_2H_5)_2$) (X = NH_2, $NHCH_3$, $N(C_2H_5)_2$) (X = NH_2, $NHCH_3$, $N(C_2H_5)_2$)

It is of interest to note that on treatment of 2-ethylthiopyrimidines [7] [VII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] with 30% hydrogen peroxide, pyrimidine sulfones were not isolated, while 2-ethylthio-5--methylpyrimidines [XI, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] under the same conditions form pyrimidine sulfones in varying yields. Apparently, in the presence of a CH_3 group in position 5 of the pyrimidine ring, the rate of oxidation of 2-ethylthiopyrimidines by hydrogen peroxide decreases, and in this case the oxidation may stop at the pyrimidine sulfone [XII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] stage.

We decided also to conduct several experiments showing the dependence of the yield of pyrimidine sulfones [XII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$] on the hydrogen peroxide concentration and the relation between the hydrogen peroxide concentration and the rate of replacement of the 2-ethanesulfonyl group in pyrimidine sulfones [XII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$]. The results of these experiments are shown in Tables 1, 2, and 3.

It has been established that 2-ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl) on reaction with hydrogen peroxide forms 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl) in various yields depending on the hydrogen peroxide concentration. When the latter was 17.5%, the yield of pure pyrimidine sulfone (XII, X = Cl) amounted to 82.5%; no by-products were isolated in this case. If the hydrogen peroxide concentration is gradually decreased, the yield of pyrimidine sulfone also gradually decreases, and the amount of original alkylthiopyrimidine (XI, X = Cl) in the reaction products increases. With 3% hydrogen peroxide the yield of pyrimidine sulfone was 25.3%, and the recovery of original alkylthiopyrimidine (XI, X = Cl) amounted to 70%. The use of hydrogen peroxide having a concentration greater than 17.5% leads to a decrease in the yield of pyrimidine sulfone (XII, X = Cl). With 20% hydrogen peroxide, 4-chloro-5-methylpyrimidine (XIII, X = Cl) was isolated from the reaction products in 20% yield. With 24.8% hydrogen peroxide another reaction product was obtained – thymine (XIV, X = OH) – in 52% yield. With 36% hydrogen peroxide, 4-chloro-5-methylpyrimidine (XIII, X = Cl) was isolated in 24% yield and thymine in 75% yield; no pyrimidine sulfone was obtained in this experiment.

2-Ethylthio-4-ethoxy-5-methylpyrimidine (XI, X = OC_2H_5) on treatment with hydrogen peroxide gave 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine (XII, X = OC_2H_5); the yield of which also depended on the hydrogen peroxide concentration. With 16.5% hydrogen peroxide the pyrimidine sulfone (XII, X = OC_2H_5) was obtained in 78.5% yield, while the quantity of recovered original alkylthiopyrimidine (XI, X = OC_2H_5) amounted to 15%. As the hydrogen peroxide concentration was decreased, the yield of pyrimidine sulfone fell, and the recovery of original alkylthiopyrimidine increased (XI, X = OC_2H_5). The yield of pyrimidine sulfone also decreased with increase in the hydrogen peroxide concentration. On treatment with 17.5% hydrogen peroxide the reaction involved the 2-methanesulfonyl group of the pyrimidine sulfone, as a result of which 2-hydroxy-4-ethoxy-5-methylpyrimidine (XIV, X = OC_2H_5) was obtained in 15% yield. With 21.5% hydrogen peroxide, thymine was found in 10.7% yield in the reaction products. On treatment with 36% hydrogen peroxide, 2-hydroxy-4-ethoxy-5-methylpyrimidine was obtained in 30% yield and thymine in 65.5% yield, while the pyrimidine sulfone was not obtained.

The yield of 2-ethanesulfonyl-4-amino-5-methylpyrimidine (XII, X = NH_2), formed on treatment of 2-ethylthio-4-amino-5-methylpyrimidine (XI, X = NH_2) with hydrogen peroxide, also varied in dependence on the hydrogen peroxide concentration. In experiments with 20% hydrogen peroxide the yield of pyrimidine sulfone (XII, X = NH_2) was 85.7%, while the recovery of original alkylthiopyrimidine (XI, X = NH_2) amounted to 8%. As the hydrogen peroxide concentration decreased, the yield of pyrimidine sulfone sharply fell, and the recovery of original alkylthiopyrimidine (XI, X = NH_2) rose. The yield of pyrimidine sulfone also decreased with increase in the hydrogen peroxide concentration, while the yield of 2-hydroxy-4-amino-5-methylpyrimidine was obtained in 18% yield. With 36% hydrogen peroxide the yield of 2-hydroxy-4-amino-5-methylpyrimidine was 65.6%; the pyrimidine sulfone was not obtained in this case.

Thus, as a result of the work carried out, it has been established that hydrogen peroxide oxidizes 2-alkylthio-5-methylpyrimidines [XI, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, or $N(C_2H_5)_2$]. At a certain hydrogen peroxide concentration the oxidation may stop at the 2-alkanesulfonyl-5-methylpyrimidine stage [XII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, $N(C_2H_5)_2$]. On treatment with more concentrated hydrogen peroxide the 2-alkanesulfonyl group was replaced by a hydroxyl group; i. e., pyrimidine sulfones [XII, X = Cl, OCH_3, OC_2H_5, NH_2, $NHCH_3$, $N(C_2H_5)_2$] proved unstable in the presence of excess hydrogen peroxide; the $-\text{S}-\overset{|}{\underset{\|}{\text{C}}}$ bond was easily broken.

Derivatives of uracil, thymine, and cytosine are often found among the products of metabolism. Organic peroxides are usually present in biological systems. It may be assumedthat similar intermolecular oxidation-reduction occurs in biological systems. Alkylthiopyrimidines and pyrimidine sulfones can scarcely be present in biological systems.

In the future the authors intend to study the action of organic peroxides on alkylthiopyrimidines.

EXPERIMENTAL

Syntheses of Alkylthiopyrimidines

2-Ethylthio-4-hydroxy-5-methylpyrimidine (XI, X = OH) was prepared thru the condensation of the sodium derivative of ethyl α-formylpropionate with ethyl pseudothiourea hydrobromide according to the directions of Wheeler and Johnson [8]. A yellowish, crystalline substance with m.p. 154-155° (from water) was obtained. The sodium derivative of the ethyl α-formylpropionate was synthesized according to the directions of Harkins and Johnson [9].

2-Ethylthio-4-chloro-5-methylpyrimidine (XI, X = Cl) was prepared according to the directions of Wheeler and Johnson [8]; b.p. 135° (14 mm).

2-Ethylthio-4-methoxy-5-methylpyrimidine (XI, X = OCH_3). 2-Ethylthio-4-chloro-5-methylpyrimidine (94.3 g, or 0.5 mole) was added with stirring to a cooled solution of sodium methoxide in methyl alcohol (0.5 mole with a slight excess in 200 ml of methyl alcohol), which was cooled to 5° beforehand. The mixture was left overnight. As much water was then added as was required for solution of the sodium chloride precipitate. The mixture was treated with ether, the ether extract was dried with anhydrous sodium sulfate and filtered, and the solvent was driven off. The substance obtained was purified by distillation in vacuo; b. p. 104-105° (4 mm). Yield, 85 g (92.4%).

Found %: N 15.15, 15.18. $C_8H_{12}ON_2S$. Calculated %: N 15.21.

2-Ethylthio-4-ethoxy-5-methylpyrimidine (XI, X = OC_2H5) was synthesized according to the directions of Sprague and Johnson [1]; b.p. 108° (3 mm).

2-Ethylthio-4-amino-5-methylpyrimidine (XI, X = NH_2) was prepared by the method of Wheeler and Johnson [8]; m.p. 96-97°.

2-Ethylthio-4-methylamino-5-methylpyrimidine (XI, X = $NHCH_3$). 2-Ethylthio-4-chloro-5-methylpyrimidine (9.43 g, or 0.05 mole) was added to 15 g of 33% aqueous methylamine solution. The mixture was heated in a sealed tube at 100° for 6 hours. After cooling, the reaction mass was a yellowish oil mixed with a certain amount of a solid substance crystallizing in the form of leaflets. The solid substance was filtered off. After complete removal of the solvent from the mother liquor in a vacuum desiccator, a solid substance was obtained. Both portions of the substance were combined and recrystallized from absolute ether. White leaflets with m.p. 58.5-60° were obtained. On standing in air for 2-3 hours the crystals deliquesced, changing to an oil.

Hydrochloride. As the crystals obtained above very readily deliquesced in air, the substance was heated with a small volume of alcoholic hydrochloric acid solution, after which the hydrochloride precipitated in the form of white leaflets. The hydrochloride was recrystallized from anhydrous alcohol; m.p. 228-229°. It did not deliquesce in air. Qualitative analysis showed the presence of sulfur, nitrogen, and chlorine.

Found %: N 19.08, 19.12; S 16.12, 16.26. $C_8H_{13}N_3S \cdot HCl$. Calculated %: N 19.5; S 16.14.

2-Ethylthio-4-diethylamino-5-methylpyrimidine [XI, X = $N(C_2H_5)_2$]. 2-Ethylthio-4-chloro-5-methylpyrimidine (9.43 g, or 0.05 mole) and diethylamine (10 ml, or 0.14 mole) were dissolved in 14 ml of ethyl alcohol. The mixture was heated to 100° for 6 hours. After cooling, the diethylaminopyrimidine separated in the form of leaflets; the solution was a viscous oil. The crystals were filtered off, and the viscous, oily liquid was evaporated in a vacuum desiccator. In the residue a yellowish, crystalline substance was obtained. The crystals were combined and recrystallized from anhydrous alcohol; m.p. 75-76°. On standing in air, the crystals quickly changed to an oil.

Hydrochloride. Since the substance quickly deliquesced in air, it was heated with alcoholic hydrochloric acid solution to obtain the corresponding hydrochloride. The white, crystalline hydrochloride, after recrystallization from ethyl alcohol, had m.p. 223-224°.

Found %: N 17.52, 16.64; Cl 13.96, 13.97. $C_{11}H_{19}N_3S \cdot HCl$. Calculated %: N 16.06; Cl 13.55.

Action of Hydrogen Peroxide on Alkylthiopyrimidines

1 Action of hydrogen peroxide on 2-ethylthio-4-chloro-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-chloro-5-methylpyrimidine (XII, X = Cl). 2-Ethylthio-4-chloro-5-methylpyrimidine (4 g, or 0.021 mole) was dissolved in 5 ml of ethyl alcohol. The solution was heated in a water bath. To the hot solution was added 5 ml of 30% hydrogen peroxide solution (0.044 mole). The violent reaction was finished within 20 minutes. On cooling the reaction mixture to room temperature a voluminous mass of white, crystalline material separated. The crystalline product was heated to boiling with ethyl acetate, and the undissolved material was filtered out from the hot solution (and saved for the following experiment). When the hot ethyl acetate solution was cooled, 2-ethanesulfonyl-4-chloro-5-methylpyrimidine separated out. The presence of nitrogen, chlorine, and sulfur in the compound was established by qualitative analysis. The substance melted at 65-66°. Sprague and Johnson [1] give m. p. 67.5-68°. A mixture of the obtained substance with the pyrimidine sulfone prepared according to the method of Sprague and Johnson [1] by treatment of 2-ethylthio-4-chloro-5-methylpyrimidine with chlorine and water showed no melting-point depression.

Found %: N 12.74, 12.71; S 14.51, 14.83; Cl 16.56, 16.60. $C_7H_9O_2N_2SCl$. Calculated %: N 12.70; S 14.53; Cl 16.07.

Isolation of 4-chloro-5-methylpyrimidine (XIII, X = Cl). The residue which had not dissolved in hot ethyl acetate was recrystallized from 50% ethyl alcohol. 4-Chloro-5-methylpyrimidine separated out in the form of white crystalline granules, m.p. 62-63°. The mother liquor was saved for the following experiment.

Found %: N 22.02, 21.78; Cl 27.88, 28.04. $C_5H_5N_2Cl$. Calculated %: N 21.80; Cl 27.59.

Isolation of thymine (XIV, X = OH). After 4 hours a white, crystalline substance separated out from the remaining mother liquor in the form of short needles with m.p. 321° (dec.). Fischer [10] and Johnson [11] give the same melting point.

Found %: N 22.22, 22.32. $C_5H_6O_2N_2$. Calculated %: N 22.23

2. Action of hydrogen peroxide on 2-ethylthio-4-methoxy-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-methoxy-5-methylpyrimidine (XII, X = OCH_3). 2-Ethylthio-4-methoxy-5-methylpyrimidine (0.025 mole) was dissolved in 5 ml of ethyl alcohol, and the solution was heated in a water bath. To the hot solution was added a certain quantity of 30% hydrogen peroxide (0.05 mole). The white, crystalline substance which separated out as a result of the reaction was heated to boiling with ethyl formate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-methoxy-5-methylpyrimidine separated out from the ethyl formate solution; it was recrystallized from the same solvent. M.p. 67.5-68°.

Found %: N 12.88, 12.90; S 14.65, 14.77. $C_8H_{12}O_3N_2S$. Calculated %: N 12.96; S 14.83.

Isolation of 2-hydroxy-4-methoxy-5-methylpyrimidine (XIV, X = OCH_3). The insoluble fraction obtained above was heated to boiling with methyl alcohol and separated into 2-hydroxy-4-methoxy-5-methylpyrimidine and thymine (not purified). The first substance was recrystallized from methanol; it melted at 182-183°.

Found %: N 19.11, 19.32, $C_6H_8O_2N_2$. Calculated %: N 20.00.

The unpurified thymine was recrystallized from water. M.p. 321° (dec.).

3. Action of hydrogen peroxide on 2-ethylthio-3-ethoxy-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine (XII, X = OC_2H_5). 2-Ethylthio-4-ethoxy-5-methylpyrimidine (0.025 mole) was heated in a water bath with a certain quantity of 30% hydrogen peroxide (0.05 mole) in 5 ml of ethyl alcohol. The white, crystalline substance formed in the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction . 2-Ethanesulfonyl-4-ethoxy-5-methylpyrimidine separated out from the ethyl acetate solution; it was purified by recrystallization from the same solvent; m.p. 67-68°. Sprague and Johnson [1] give the same melting point.

Found %: S 12.90, 13.98. $C_9H_{14}O_3N_2S$. Calculated %: S 13.93.

The insoluble part was fractionated, recrystallized from water, and separated into two compounds – 2-hydroxy-4-ethoxy-5-methylpyrimidine and thymine. The 2-hydroxy-4-ethoxy-5-methylpyrimidine (XIV, X = OC_2H_5), after recrystallization from water, had m.p. 212-213°. Sprague and Johnson [2] give the same melting point.

Found %: N 18.08, 18.10. $C_7H_{10}O_2N_2$. Calculated %: N 18.18.

The thymine was recrystallized from water. M.p. 321° (dec.).

4. Action of hydrogen peroxide on 2-ethylthio-4-amino-5-methyl-pyrimidine. Isolation of 2-ethanesulfonyl-4-amino-5-methylpyrimidine (XII, X = NH_2). 2-Ethylthio-4-amino-5-methylpyrimidine (0.02 mole) was heated in a water bath with a certain quantity of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline product which separated out as a result of the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-amino-5-methylpyrimidine, which separated out from the ethyl acetate solution, was recrystallized from the same solvent. M.p. 135-136.5°.

Found %: S 15.82, 15.86. $C_7H_{11}O_2N_3S$. Calculated %: S 15.94.

Isolation of 2-hydroxy-4-amino-5-methylpyrimidine hydrochloride. The insoluble fraction obtained above was heated with ethyl alcohol containing hydrogen chloride. 2-Hydroxy-4-amino-5-methylpyrimidine hydrochloride, m.p. 288-290° (dec.), separated out from the cooled solution. Wheeler and Johnson [8] give m.p. 288° (with effervescence). Sprague and Johnson [2] give m.p. 288-290°.

Found %: N 26.15, 26.22. $C_5H_7ON_3 \cdot HCl$. Calculated %: N 26.02.

5. Action of hydrogen peroxide on 2-ethylthio-4-methylamino-5-methylpyrimidine. Isolation of 2-ethanesulfonyl-4-methylamino-5-methylpyrimidine (XII, X = $NHCH_3$). 2-Ethylthio-4-methylamino-5-methylpyrimidine (0.02 mole) was heated to boiling in a water bath with a certain quantity of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline product formed in the reaction was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-methylamino-5-methylpyrimidine separated out from the ethyl acetate; it was recrystallized from the same solvent. M. p. 138-140°.

Found %: N 19.44, 19.46; S 14.89, 14.92. $C_8H_{13}O_2N_3S$. Calculated %: N 19.53; S 14.90.

Isolation of 2-hydroxy-4-methylamino-5-methylpyrimidine (XIV, X = $NHCH_3$). The fraction which had not dissolved in ethyl acetate was dissolved in 80% ethyl alcohol; on cooling of the solution 2-hydroxy-4-methylamino-5-methylpyrimidine, m.p. 235°, separated out.

Found %: N 30.22, 30.32. $C_6H_9ON_3$. Calculated %: N 30.22.

6. Action of hydrogen peroxide on 2-ethylthio-4-diethylamino-5-methylpyrimidine Isolation of 2-ethanesulfonyl-4-diethylamino-5-methylpyrimidine [XII, X = $N(C_2H_5)_2$]. 2-Ethylthio-4-diethylamino-5-methylpyrimidine (0.02 mole) was heated in a water bath with a certain volume of 30% hydrogen peroxide (0.045 mole) in 3 ml of ethyl alcohol. The white, crystalline reaction product was heated to boiling with ethyl acetate and divided into a soluble and an insoluble fraction. 2-Ethanesulfonyl-4-diethylamino-5-methylpyrimidine separated out from the solution; it was recrystallized from the same solvent. M.p. 139-140°.

Found %: N 16.92, 16.95; S 12.94, 12.92. $C_{11}H_{19}O_2N_3S$. Calculated %: N 16.34; S 12.46.

TABLE 1

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-chloro-5-methylpyrimidine on the Concentration of the Former

Hydrogen peroxide concentration (in %)	Yield of reaction products (in %)			Recovery of original alkylthiopyrimidine (in %)
	2-ethanesulfonyl-4-chloro-5-methylpyrimidine	4-chloro-5-methylpyrimidine	thymine	
3	25.3	—	—	70.0
10	38.5	—	—	58.0
15.5	60.0	—	—	25.5
17.5	82.5	—	—	—
20	70.5	20.0	—	—
23.6	64.5	25.5	—	—
24.8	30.4	15.0	52	—
30	26.0	16.4	53.5	—
36	—	24.0	75.0	—

Isolation of 2-hydroxy-4-diethylamino-5-methylpyrimidine [XIV, X = $N(C_2H_5)_2$]. The fraction insoluble in ethyl acetate was dissolved in 80% ethyl alcohol, from which 2-hydroxy-4-diethylamino-5-methylpyrimidine, m.p. 232°, separated out on cooling.

Found %: N 23.75, 23.79. $C_9H_{15}ON_3$. Calculated %: N 23.20.

Dependence of the Action of Hydrogen Peroxide on Alkylthiopyrimidines on its Concentration

Reactions of 2-ethylthio-4-R-5-methylpyrimidines (R = Cl, OC_2H_5, NH_2) with hydrogen peroxide of various concentrations were carried out. It was established that the yield of pyrimidine sulfones and the recovery of the original pyrimidine derivatives also depended on the hydrogen peroxide concentration. The results obtained are given in Tables 1-3.

TABLE 2

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-ethoxy-5-methylpyrimidine on the Concentration of the Former

Hydrogen peroxide concentration (in %)	Yield of reaction products (in %)			Recovery of original alkylthiopyrimidine (in %)
	2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine	2-hydroxy-4-ethoxy-5-methylpyrimidine	thymine	
3	22.4	—	—	75.0
10	40.2	—	—	50.4
15	56.6	—	—	30.0
16.5	78.5	—	—	15.0
17.5	70.0	15	—	—
21.5	60.2	12.0	10.7	—
26.4	28.8	19.2	50.5	—
30	25.0	20.2	50.0	—
36	—	30	65.5	—

TABLE 3

Dependence of the Action of Hydrogen Peroxide on 2-Ethylthio-4-amino-5-methylpyrimidine on the Concentration of the Former

Hydrogen peroxide concentration (in %)	Yield of reaction product (in %)		Recovery of original alkylthiopyrimidine (in %)
	2-ethanesulfonyl-4-amino-5-methylpyrimidine	2-hydroxy-4-amino-5-methylpyrimidine	
3	25	—	70
10	35.5	—	60
15	52.5	—	30
20	85.7	—	8
23.6	78	18	—
24.8	62	21.5	—
26.4	550	42.5	—
30	45.5	41	—
36	—	85.6	—

The analyses for nitrogen, given in the present work, were performed by Ch'ao Ch'a-lung, Wang Tien-jeng and Fang Weng-Ch'ai for which the authors sincerely thank them.

SUMMARY

1. 2-Ethylthio-4-chloro-5-methylpyrimidine on treatment with 30% hydrogen peroxide in ethyl alcohol formed 2-ethanesulfonyl-4-chloro-5-methylpyrimidine, 4-chloro-5-methylpyrimidine, and 2-hydroxy-4-chloro-5-methylpyrimidine (which changed to thymine on recrystallization from water or dilute ethyl alcohol).

2. 2-Ethylthio-4-methoxy- (or -ethoxy-)5-methylpyrimidine on reaction with 30% hydrogen peroxide in ethyl alcohol gave 2-ethanesulfonyl-4-methoxy- (or -ethoxy-)5-methylpyrimidine, 2-hydroxy-4-methoxy- (or -ethoxy-)5-methylpyrimidine, and thymine.

3. 2-Ethylythio-4-amino-(-N-methylamino- or -N-diethylamino-)5-methypyrimidine reacted with 30% hydrogen peroxide in ethyl alcohol to form 2-ethanesulfonyl-4-amino- (N-methylamino- or -N-diethylamino-) 5-methylpyrimidine and 2-hydroxy-4-amino- (-N-methylamino- and -N-diethylamino-) 5-methylpyrimidine.

4. The rate of oxidation of a 2-ethylthiopyrimidine by hydrogen peroxide is decreased if there is a CH_3 group in position 5 of the pyrimidine ring. The oxidation may stop at an intermediate stage, and in these cases pyrimidine sulfones can be isolated.

5. The yield of pyrimidine sulfones varies in dependence on the hydrogen peroxide concentration. With 17.5% hydrogen peroxide the yield of 2-ethanesulfonyl-4-chloro-5-methylpyrimidine was 82.5% With 16.5% hydrogen peroxide the yield of 2-ethanesulfonyl-4-ethoxy-5-methylpyrimidine amounted to 78.5%. With 20% hydrogen peroxide the yield of 2-ethanesulfonyl-4-amino-5-methylpyrimidine was 85.7%.

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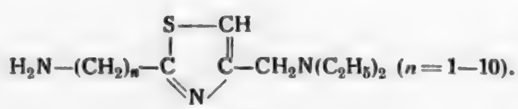
INVESTIGATIONS IN THE THIAZOLE SERIES

V. SYNTHESIS OF 2-δ-AMINO-n-BUTYL-4-N-DIETHYLAMINO-METHYLTHIAZOLE

Ch'ih Yueh-fon and Zin Shih-yung

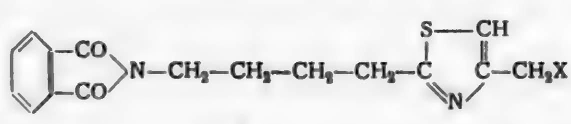
In previous papers [1, 2] we put forward a method of synthesizing 2-aminoalkyl-N-diethylaminomethylthiazole (I).



(I)

Similar alkylenediamines, containing a thiazole ring, may be active physiologically. S. G. Fridman [3] showed that N-β-dimethylaminoethyl-N-benzyl-2-amino-4-methylthiazole had an anthihystaminic effect. The introduction of a thiazole ring into β-phenylethylamine and its derivatives considerably lowers their toxicity [4, 5]. Goldberg (6) noted the antibacterial acitivity of 2-ω-aminoalkylthiazole derivatives. It was quite logical to consider that the toxicity of alkylenediamines would be reduced by the introduction of a thiazole ring.

In the present work we describe the synthesis of 2-δ-amino-n-butyl-4-N-diethylaminoethylthiazole (I, n = 4). The thioamide of δ-phthalimido-n-valeric acid was condensed with α, γ-dichloroacetone to form 2-δ-phthalimido-n-butyl-4-chloromethylthiazole (II, X = Cl), which was reacted with diethylamine to give 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole (IIb, X = $N(C_2H_5)_2$).



(II)

(IIa), X = Cl;
(IIb), X = $N(C_2H_5)_2$.

The product obtained was treated with hydrazine hydrate by the method of Ing and Manske [7]. This removed the phthalyl group to give the required 2-δ-aminobutyl-4-N-diethylaminomethylthiazole (I, n = 4).

EXPERIMENTAL

δ-Bromovaleronitrile. The 1,4-dibromobutane required for the synthesis was prepared from tetramethylene glycol by passing hydrogen bromide through it. The tetramethylene glycol was prepared by reducing diethyl succinate with sodium in ethyl alcohol. For the preparation of δ-bromovaleronitrile, 1,4-dibromobutane was treated with potassium cyanide by the method Goldberg and Kelly [8] described for the synthesis of γ-bromobutyronitrile.

1,4-Dibromobutane (65 g) was dissolved in 95 ml of ethyl alcohol and to the solution was added potassium cyanide solution (24 g of potassium cyanide in 48 ml of water) dropwise with heating and stirring. The addition of the potassium cyanide solution required about an hour and half and after this, the reaction mixture was heated and stirred for a further 1 hour. The cooled solution was poured into 240 ml of water and extracted 3 times with chloroform (45 ml portions). The chloroform extract was dried with anhydrous sodium sulfate and filtered, the solvent removed and the residual oil distilled in vacuum. The following fractions were collected: 1st b. p. 80-86° (4 mm), 14 g, unreacted 1,4-dibromobutane; 2nd b. p. 92-98° (4 mm), 12.5 g, (25.6%), δ-bromo-n-valeronitrile; 3rd b. p. 120-132° (4 mm), 4 g, 1,4-dicyanobutane.

δ-Phthalimido-n-valeronitrile. Potassium phthalimide (12 g) and δ-bromo-n-valeronitrile (9.5 g) were mixed with 35 ml of anhydrous ethyl alcohol and heated with stirring for 10 hours on an oil bath at 110-120° The solvent (about 20 ml) was partly evaporated and the residual liquid poured into 50 ml of water. The crystalline precipitate formed was recrystallized from ethyl alcohol. A fine, colorless powder with m. p. 74-76° was obtained. The yield of δ-phthalimido-n-valeronitrile was 8.1 g (60.5%).

Found %: N 12.18, 12.42. $C_{13}H_{12}O_2N_2$. Calculated %: N 12.28.

Thioamide of δ-phthalimido-n-valeric acid. Experiment 1. δ-Phthalimido-n-valeronitrile (1.2 g) was mixed with an alcohol solution of ammonium bisulfide (prepared by dissolving 3.0 g of NH_3 and 0.26 g of H_2S in 7.2 ml of C_2H_5OH). The mixture was placed in a sealed tube, which was shaken periodically for 48 hours, and then the crystalline thioamide of δ-phthalimido-n-valeric acid with m. p. 145-146° was isolated. The yield was 34%.

Found %: N 10.19, 10.23; S 12.20. $C_{13}H_{12}O_2N_2S$. Calculated %: N 10.69; S 12.23.

Evaporation of the mother liquors and cooling yielded a compound with m.p. 217-218.5°, which contained nitrogen but no sulfur. It was assumed that this substance was δ-phthalimido-n-valeramide.

Found %: N 16.84, 16.61. $C_{13}H_{15}O_2N_3$. Calculated %: N 17.14.

Experiment 2. δ-Phthalimido-n-valeronitrile (10 g) was dissolved in 50 ml of anhydrous ethyl alcohol, to which was added tri-(β-ethanol)-amine (0.5 g). The solution was heated to 40° and a stream of dry hydrogen sulfide passed in for a period of 53 hours. On cooling, the solution yielded a crystalline substance with m. p. 112-120°. The yield of crude product was 7.8 g. The substance was purified by recrystallization from 50% ethyl alcohol. It crystallized in the form of a colorless finely crystalline powder with m.p. 142-144°. The yield of pure thioamide of δ-phthalimido-n-valeric acid was 5.8 g (50.5%).

Found %: N 10.28, 9.96; S 12.32. $C_{13}H_{14}O_2N_2S$. Calculated %: N 10.69; S 12.23.

2-δ-Phthalimido-n-butyl-4-chloromethylthiazole (II, X = Cl). δ-Phthalimido-n-valerothioamide (3.7 g) and α, γ-dichloroacetone (1.8 g) were mixed with 18 ml of anhydrous alcohol and heated for 3 hours. The solution was kept overnight in a refrigerator and then the colorless, crystalline substance with m.p. 78-81° was isolated. The yield of crude product was 2.3 g. The substance was purified by recrystallization from anhydrous ethyl alcohol. We obtained fine, microscopic crystals with m.p. 82-83°. The yield of pure 2-δ-phthalimido-n-butyl-4-chloromethylthiazole was 2.8 g (38.1%).

Found %: N 8.38, 9.03; S 10.14; Cl 10.02. $C_{16}H_{15}O_2N_2SCl$. Calculated %: N 8.37; S 9.58; Cl 10.59.

The mother liquor was concentrated under reduced pressure until the separation of a white, crystalline substance (m.p. 152-163°) began. The substance obtained, which was apparently the hydrochloride of 2-δ-phthalimido-n-butyl-4-chloromethylthiazole, dissolved in sodium bicarbonate with the evolution of CO_2. The solution obtained was extracted with chloroform. The extract was dried and the solvent distilled off. The sirupy residue was kept in ice overnight and yielded a small amount of a solid substance, which was recrystallized from ethyl alcohol to give microscopic crystals with m.p. 81-83°.

2-δ-Phthalimido-n-butyl-4-N-diethylaminomethylthiazole [II, X = $N(C_2H_5)_2$]. 2-δ-Phthalimido-n-butyl-4-chloromethylthiazole (1.5 g) and diethylamine (1.5 g) were dissolved in 50 ml of anhydrous ethyl alcohol. The solution was boiled for 6 hours. After removal of the ethyl alcohol, the residue was neutralized with soda solution and extracted three times with ethyl ether (5 ml of ethyl ether in each portion). The ether extract was dried with potash, filtered and the solvent distilled off. Attempts to purify the residual oil by distillation at a residual pressure of 100μ (bath temperature 300-310°) were unsuccessful.

For preparation of the hydrochloride, the crude 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole was dissolved in a small volume of anhydrous ethanol and a 5% solution of hydrochloric acid in ethanol added dropwise until the pH of the solution equalled 4. Then ethyl ether was added to the alcohol solution dropwise until a slight turbidity appeared. The solution was kept in a refrigerator overnight, when it deposited fine, microscopic crystals, which were recrystallized from a mixture of alcohol and ether to form small leaves with m.p 105-106°.

Found %: N 9.87; S 7.38; Cl 8.41. $C_{20}H_{25}O_2N_3Cl \cdot HCl$. Calculated %: N 10.31; S 7.86; Cl 8.70.

2-δ-Amino-n-butyl-4-N-diethylaminomethylthiazole (I, n = 4). 2-δ-Phthalimido-n-butyl-4-N-diethylaminomethylthiazole (3.7 g) was dissolved in 80 ml of ethyl alcohol, to which was added 1 ml of hydrazine hydrate. The mixture was heated on a water bath under reflux for 1.5 hours. The ethyl alcohol was then removed under reduced pressure and the residual oil cooled and acidified with 6 N hydrochloric acid. The phthalyl hydrazide separated as a semisolid precipitate, which was filtered off. The filtrate was treated with 50 ml of 40% sodium hydroxide solution to liberate a yellow oil, which floated on the surface. To the oil, which had been separated from the aqueous solution, was added barium oxide (7 g) and the mixture heated for 1 hour on a water bath. After being cooled, the mixture was extracted three times with ether, using 20 ml portions of ether. The ether extracts were dried with anhydrous potash, filtered and the solvent evaporated. The residual oil was purified by vacuum distillation. The pure 2-δ-amino-n-butyl-4-N-diethylaminomethylthiazole boiled at 149-150° (6 mm). Yield was 0.9 g (37%).

Found %: N16.84, 17.07; S 12.93. $C_{12}H_{23}N_3S$. Calculated %: N 17.42; S 13.29.

The analyses given in this article were performed bv Ch'ao Ch'ang-ling, Wang Tieh-jeng, Ping Shu-k'uei, Wang We-ch'e, to whom the authors are extremely grateful.

SUMMARY

1. The reaction of δ-bromo-n-valeronitrile with potassium phthalimide in ethyl alcohol lead to δ-phthalimido-n-valeronitrile, which was converted into δ-phthalimido-n-valerothioamide by reaction with ammonium bisulfide in ethyl alcohol and also by reaction with hydrogen sulfide in ethyl alcohol in the presence of tri-(β-ethanol)-amine.

2. δ-Phthalimido-n-valerothioamide was condensed with α, γ-dichloroacetone in ethyl alcohol to form 2-δ-phthalimido-n-butyl-4-chloromethylthiazole.

3. 2-δ-Phthalimido-n-butyl-4-chloromethylthiazole reacted with diethylamine to from 2-δ-phthalimido-n-butyl-4-N-diethylaminomethylthiazole and when this was heated with hydrazine hydrate, the phthalyl group was removed to yield the free amine—2-δ-amino-n-butyl-4-N-diethylaminomethylthiazole.

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* See C.B. Translation.

AN ANOMALOUS REACTION OF α-HALO KETONES WITH ESTERS OF PHOSPHOROUS ACID

VII. REACTIONS OF ESTERS OF PHOSPHOROUS ACID WITH CHLORINATED DERIVATIVES OF β-DIKETONES

A. N. Pudovik and L. G. Biktimirova

Reactions of esters of phosphorous acid with brominated derivatives of some β-dicarbonyl compounds have been studied by B. A. Arbuzov and N. P. Bogonostseva [1]. These workers demonstrated that in the reaction of triethyl phosphite with dibenzoylbromomethane, tribenzoylbromomethane and bromoindanedione there are formed, respectively, dibenzoylmethane, tribenzoylmethane and indanedione. From the reaction with tribenzoylbromomethane, in addition to the tribenzoylmethane, there was isolated a fraction, the constants of which correspond to those of triethyl phosphate. The authors regard the radical mechanism of this reaction to be the most probable one: the free radicals of dibenzoylmethyl, tribenzoylmethyl and indanedionyl, which are formed in the first stage of the reaction, are later reduced either by hydrogens of triethyl phosphite or those of the solvent. Kreutzkamp and Kuser [2], who studied the reaction of trialkyl phosphites with chlorobenzoylacetone and tribenzoylchloromethane, also note the formation of only the products of reduction of the latter substances – benzoylacetone and tribenzoylmethane.

We have shown in a previous study [3] that α-bromo- and α-chloro-ketones, which possess a halogen atom on the primary carbon atom, behave differently in their reactions with phosphites. Bromo ketones react predominantly by the scheme of the Arbuzov rearrangement with formation of phosphonoketones, while chloroketones yield mainly the unsaturated phosphate esters. As was shown in one of our previous papers [4], the reactions of triethylphosphite and triisobutyl phosphite with chloro- and dichloro derivatives of acetylacetone and acetoacetic ester proceed completely anomalously with formation of unsaturated phosphate esters.

Continuing the development of these investigations, in the present work we studied the reactions of chloro- and dichloro-substituted derivatives of acetylacetone, benzoylacetone, dibenzoylmethane and dimedone (dimethylcyclohexanedione) with various phosphites. One might assume, in accord with the previously obtained results, that in all these reactions the unsaturated phosphate ester would form as either the intermediate or as the final products.

Reactions of chloro- and dichloroacetone with trimethyl phosphite and tri-n-butyl phosphite proceed completely anomalously: there were obtained, in yields of 60-80%, the corresponding 1-methyl-1-buten-3-onyl dialkyl or 1-methyl-2-chloro-1-buten-3-onyl dialkyl esters of phosphoric acid (see table, substances I-IV).

$$\underset{\substack{|\\ O\\ |\\ O=P(OR)_2}}{CH_3-C}{=}CHCOCH_3 \quad (I,\ II) \qquad \underset{\substack{|\\ O\\ |\\ O=P(OR)_2}}{CH_3-C}{=}CClCOCH_3 \quad (III,\ IV) \qquad \underset{\substack{|\\ O\\ |\\ O=P(OR)_2}}{C_6H_5-C}{=}CHCOCH_3 \quad (V,\ VI)$$

(I) & (III) $R = CH_3$, (II) & (IV) $R = n\text{-}C_4H_9$, (V) $R = CH_3$; (VI) $R = C_2H_5$.

The presence of the double bond in these compounds was proved by bromination, according to McIlliney, while acetylacetone was obtained by careful hydrolysis of (I). It is interesting to note that compound (I) after

Constants of 1-Methyl-1-buten-3-onyl Dialkyl and 1-Methyl-2-chloro-1-buten-3-onyl Dialkyl Esters of Phosphoric Acid $R'-C(-O-P(O)(OR)_2)=CXCOR''$

	Names of compounds	Significance in the formula				Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Content (in %)			
											phosphorus		chlorine	
		R	R′	R″	X				found	calc.	found	calc.	found	calc.
(I)	1-Methyl-1-buten-3-onyl dimethyl ester of phosphoric acid	CH_3	CH_3	CH_3	H	103—104° (2)	1.2040	1.4572	46.00	46.06	14.40, 14.83	14.90	—	—
(II)	1-Methyl-1-buten-3-onyl di-n-butyl ester of phosphoric acid	n-C_4H_9	CH_3	CH_3	H	125—127 (1)	1.0503	1.4510	74.86	73.77	10.64, 10.64	10.61	—	—
(III)	2-Chloro-1-methyl-1-buten-3-onyl dimethyl ester of phosphoric acid	CH_3	CH_3	CH_3	Cl	115 (2)	1.3085	1.4710	51.79	50.93	12.71, 12.53	12.781	15.38	14.64
(IV)	2-Chloro-1-methyl-1-buten-3-onyl di-n-butyl ester of phosphoric acid	n-C_4H_9	CH_3	CH_3	Cl	138—139 (2)	2.1202	1.4615	79.66	78.64	9.56, 9.91	9.49	11.31	10.87
(V)	1-Phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid	CH_3	C_6H_5	CH_3	H	138—139 (1)	1.2278	1.5262	67.52	65.55	11.68, 12.02	11.48	—	—
(VI)	1-Phenyl-1-buten-3-onyl diethyl ester of phosphoric acid	C_2H_5	C_6H_5	CH_3	H	170—172 (2)	1.1611	1.5135	77.20	74.78	10.11	10.40	—	—
(VII)	2-Chloro-1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid	CH_3	C_6H_5	CH_3	Cl	156—157 (2.5)	1.2969	1.5223	71.64	70.51	10.48	10.18	11.17	11.66
(VIII)	1-Phenyl-2-benzoylethenyl diethyl ester of phosphoric acid	C_2H_5	C_6H_5	C_6H_5	H	208 (3)	—	1.5490	—	—	8.88	8.61	—	—

two months of storage at room temperature acquired a dark brown color and the odor of acetylacetone. On distillation of this material there was indeed isolated some 10% by weight of acetylacetone; the remainder was the unchanged product. Analogous unsaturated phosphate esters, containing ethyl and n-butyl radicals, were unchanged after storage for several months. In running the reactions of chlorobenzoylacetone with trimethyl and triethyl phosphite there were obtained in 70-80% yields: 1-phenyl-1-buten-3-onyl dimethyl (V) and 1-phenyl-1-buten-3-onyl diethyl (VI) esters of phosphoric acid.

The presence of the double bonds in these esters was proved by bromination. From the low-boiling fractions, obtained during the isolation of (V) and (VI), there separated after a short interval of standing a small quantity of crystals which turned out to be benzoylacetone (m.p. 60-61°; mixed melting point 60°). The amount of benzoylacetone increased with a slow distillation or with higher temperature. Compounds (V) and (VI) acquire a brown color after only a few days storage; during their distillation there distills a considerable amount of benzoylacetone. One may suppose that the facile decomposition of (V) and (VI) is connected with their hydrolysis by the action of atmospheric moisture. Actually a brief heating of compounds (V) and (VI) with water leads to a total hydrolysis and quantitative formation of benzoylacetone. However, special measures taken for the protection of (V) and (VI) from moisture during the process of distillation and storage failed to decrease the rate of their decomposition. Heating (V) and (VI) in sealed ampoules at 150-160° for six hours leads to their almost total decomposition. Benzoylacetone is distilled in considerable amounts from the resulting dark, viscous mass. The process of thermal decomposition of (V) was followed by determination of the change of viscosity of the reaction mixture during the process of heating. Relative viscosity of (V) increases two-fold in five hours and seven-fold in twenty hours during heating of the substance in a thermostat at 155-160° in a sealed viscosimeter (both bulbs of the viscosimeter are connected by means of a sealed-in glass air tube. Measurements of viscosity were made in a thermostat at 20°. Crystallization of benzoylacetone begins during further heating and the reaction mixture, in being cooled, is transformed to a hard crystalline product saturated with a dark tar. A thermographic study of the reaction of benzoylchloroacetone with trimethyl phosphite was carried out (Fig. 1) and a thermogram of decomposition of (V) was run separately (Fig. 2).

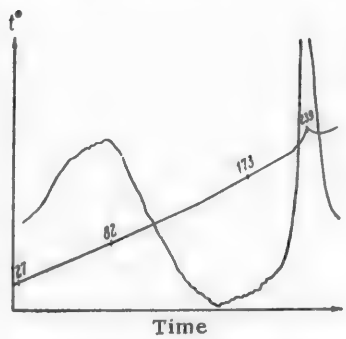


Fig. 1. Thermogram of reaction of benzoylchloroacetone with trimethyl phosphite

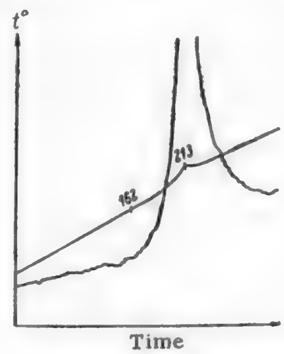
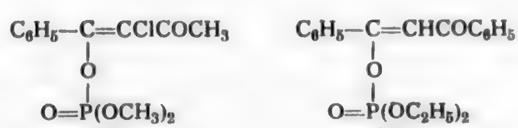


Fig. 2. Thermogram of the decomposition of 1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid (V).

On the first thermogram (Fig. 1) there were recorded two exothermic effects: the first of these corresponds to the reaction of trimethyl phosphite with benzoylchloroacetone, while the second effect, a considerably greater one, corresponds to the thermal decomposition of (V). The latter effect was recorded also in the second thermogram (Fig. 2).

From the reaction of trimethyl phosphite with dichlorobenzoylacetone there was obtained a 72% yield of (VII).



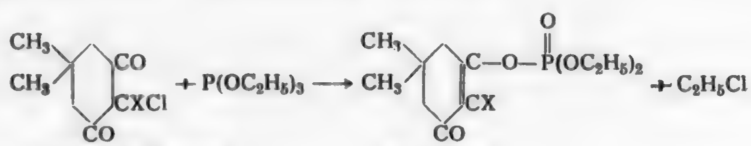
(VII) (VIII)

After heating (VII) in a sealed ampoule for four hours at 160°, with a subsequent distillation, there was isolated some chlorobenzoylacetone, with b.p. 146° (14 mm).

Fig. 3. Thermogram of decomposition of 1-phenyl-2-chloro-1-buten-3-onyl dimethyl ester of phosphoric acid (VII).

On Fig. 3 there is shown the thermogram of decomposition of (VII). The exothermic effect in this case is smaller than in decomposition of (V). As the result of the reaction of triethyl phosphite with dibenzoylchloromethane there was obtained a 20% yield of 1-phenyl-2-benzoylethenyl diethyl ester of phosphoric acid (VIII) in the form of a very viscous liquid. A considerable amount of dibenzoylmethane was also isolated.

In conclusion we reacted triethyl phosphite with chloro- and dichlorodimedones. Considerable decomposition of the reaction products was observed during their distillation. Some dimedone was isolated from the reaction with chlorodimedone and there was obtained, in poor yield and in insufficiently pure state, the 5,5-dimethyl-1-cyclohexen-3-onyl diethyl ester of phos--horic acid (IX). A small amount of crystals of dimedone precipitated from it after a brief interval of standing. Analogous results were obtained with dichlorodimedone. During the distillation of the reaction products there was isolated a considerable amount of chlorodimedone and a small amount of 2-chloro-5,5-dimethyl-1-cyclohexen-3-onyl diethyl ester of phosphoric acid (X). The presence of a double bond in (IX) and (X) was confirmed by bromination.



(IX) X=H; (X) X=Cl. (IX) & (X)

The mechanism of the thermal decomposition of the unsaturated phosphate esters prepared by us remains unclarified.

EXPERIMENTAL

The technique of running the reactions (Syntheses of I-VIII). To 0.1-0.15 mole of chloro- or dichloroacetylacetone or benzoylacetone there was added gradually an equimolar amount of a trialkyl phosphite. The reactions began immediately (or after a brief induction period) and were accompanied by a considerable thermal effect. The alkyl chloride, which formed in the reaction, was distilled during the course of the reaction. After heating an hour on a water bath the reaction mixtures were distilled in vacuum. The constants of the products prepared by us and the analytical results are shown in the table.

Thermal decomposition of 1-phenyl-1-buten-3-onyl dimethyl ester of phosphoric acid. 8.5 g of the ester was heated in a sealed ampoule for two hours at 150-160°. The liquid became dark and very viscous. As the result of distillation in vacuum there was isolated 4 g of benzoylacetone, which crystallized in the receiver, and a small amount of an uncrystallizable liquid fraction. The undistillable tarry residue in the flask weighed 3.9 g.

Reaction of triethyl phosphite with 2-chloro-5,5-dimethyl-1,3-cyclohexanedione (chlorodimedone). The reaction was run with 6 g of chlorodimedone and 5.6 g of triethyl phosphite in benzene solution. After heating for two hours on a boiling water bath, the reaction mixture was vacuum distilled. There was obtained 2.1 g of a fraction with b. p. 166-168° (10 mm), n_D^{20} 1.4781. Crystals of dimedone (m. p. 146-147°; mixed m. p. 146°) began to precipitate from this fraction as well as from low-boiling fractions.

Found %: P 10.16. $C_{12}H_{21}O_5P$. Calculated %: P 11.23.

Reaction of triethyl phosphite with 2,2-dichloro-5,5-dimethyl-1,3-cyclohexanedione (dichlorodimedone). To the solution of 13 g of dichlorodimedone in 100 ml of absolute ether there was gradually added 9.4 g of triethyl phosphite. The reaction proceeded very energetically, with boiling of the ether. After 4 hours of heating,

the ether was distilled and the residue was distilled in vacuum. After the first distillation there was obtained 10 g of a fraction with b. p. 140-155° (2.5 mm), part of which (3.5 g) crystallized on standing. The crystals turned out to be chlorodimedone (m.p. 157-158°), and no depression was observed in a mixed melting point test. After two distillations of the liquid portion there was obtained 1.3 g of 2-chloro-5,5-dimethyl-1-cyclohexene-3-onyl diethyl ester of phosphoric acid in the form of a very viscous liquid with b.p. 160-161° (2.5 mm); n_D^{20} 1.4818.

Found %: P 10.25, 10.06; Cl 11.13. $C_{12}H_{20}O_5ClP$. Calculated %: P 9.98; Cl 11.43.

The authors express their deep gratitude to A. V. Fuzhenkova for making the thermographic study.

SUMMARY

1. The reaction of esters of phosphorous acid with chloro- and dichloroacetylacetone, benzoylacetone, dibenzoylmethane and 5,5-dimethyl-1,3-cyclohexanedione (dimedone) were studied.

2. It was shown that all these reactions proceed anomalously forming the corresponding unsaturated esters of phosphoric acid, instead of following the scheme of the Arbuzov rearrangement.

3. Some of the unsaturated esters of phosphoric acid, especially those containing phenyl or cyclohexenyl residues in the composition of the unsaturated radical, suffer a cleavage on being heated and thereby form a β-dicarbonyl compound.

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THE PROBLEM OF THE BROMINATION OF CYCLIC KETONES WITH DIOXANE DIBROMIDE

I. V. Machinskaia and A. S. Podberezina

With the objective of preparing α-bromocyclohexanone, we used the method of bromination of cyclohexanone recently developed by L. A. Ianovskaia [1]. Bromination of cyclohexanone is reported [2] to give a monobromocyclohexanone in a yield of 60%.

We brominated cyclohexanone by gradual addition of the ketone to a solution of dioxane dibromide in a mixture of dioxane and absolute ether. An attempt to effect the reaction with equimolar quantities of ketone and dioxane dibromide was unsuccessful – the reaction product broke down when an attempt was made to distil it in vacuo. We observed that the orange solution of dioxane dibromide lost its color when slightly less than 0.5 mole of ketone was added to 1 mole of dioxane dibromide. In later experiments we therefore took the dioxane dibromide and ketone inthe molar ratio of 1 : 0.45. We isolated dibromocyclohexanone from the reaction mixture.

Wallach [3] previously prepared dibromocyclohexanone by the action of bromine on cyclohexanone in glacial acetic acid. He assigned to it the structure of 2,6-dibromocyclohexanone-1. The melting point of our product coincides with that of Wallach's dibromoketone.

Dibromocyclohexanone can be distilled at 4-6 mm without appreciable decomposition. We observed partial decomposition on attempting to distil it at about 40 mm, with formation of more volatile fractions which decolorized bromine water. These products of decomposition of the dibromo compound may have been assumed by L. A. Ianovskaia (who distilled the reaction product at 32 mm) to be monobromocyclohexanone.

We did not succeed in isolating monobromocyclohexanone from the reaction products. If it is formed in the above reaction, its quantity is so small that it distils completely with the first fraction which we did not investigate because the quantity was too small. We obtained the same result on reversing the order of mixing, i.e., on gradually adding a solution of dioxane dibromide to the ketone solution.

During bromination of cyclopentanone with dioxane dibromide we also observed preferential formation of a dibromide of cyclopentanone which had not previously been described.

In this case, however, we also isolated monobromocyclopentanone from the reaction mixture.

Due to the poor stability of monobromocyclopentanone, its elementary composition could not be determined. Reaction with potassium acetate in a medium of glacial acetic acid converted the monobromo compound to α-acetoxycyclopentanone whose properties were identical with those reported in the literature [4].

EXPERIMENTAL

Bromination of cyclohexanone with dioxane dibromide. 48.6 g of bromine was gradually stirred into 27 g of dioxane. Crystalline, orange dioxane dibromide was formed on cooling. To the latter was added 30 ml of dioxane and 150 ml of absolute ether followed by cyclohexanone in small portions until the reaction mixture had decolorized. This operation was accompanied by heat liberation and the precipitate of dioxane dibromide gradually dissolved. Decolorization of the solution occurred after 13.2 g of cyclohexanone had been added.

The reaction mixture was cooled to room temperature and poured in a fine stream onto ice. The reaction product was extracted with ether. The ether solution was washed with 5% sodium bicarbonate solution and then with water and dried for 1 hour with calcium chloride. The solvent was driven off and the residue distilled in vacuo to give dibromocyclohexanone with b. p. 114-116° (4 mm).* Yield 17.3 to 23.7 g (50-69%). The product crystallized after standing for a long time. After recrystallization from alcohol, it had m.p. 106-107°.

Found %: C 28.31, 28.42; H 3.48, 3.42; Br 61.75, 61.68. $C_6H_8OBr_2$. Calculated %: C 28.15; H 3.15; Br 62.44.

The experiment must be completed on the same day; otherwise the product may decompose when distilled in vacuo.

Bromination of cyclopentanone with dioxane dibromide. Mono- and dibromocyclopentanones formed on bromination of cyclopentanone with dioxane dibromide could not both be isolated from the product of a single experiment since the dibromo compound breaks down when the monobromocyclopentanone is distilled. Mono- and dibromocyclopentanones were therefore isolated in different experiments.

Monobromocyclopentanone. 80 g bromine was gradually stirred into 44 g dioxane. A mixture of 44 ml of dioxane and 150 ml of absolute ether was then run in with cooling, followed by 21 g of cyclopentanone in small portions.** The mixture was cooled to room temperature and then worked up as in the preceding experiment. Fractional distillation of the reaction product 6 mm gave two main fractions: b.p. 64-70° (14.8 g) and b.p. 70-86° (8 g).*** When the first fraction was redistilled, it came off nearly completely at 79-83° (15 mm), in agreement with the literature data for monobromocyclopentanone [5]. The yield of the latter was 36%; b.p. 64-70° (6 mm). It is extremely unstable: on standing overnight it nearly completely resinifies.

α-Acetoxycyclopentanone. α-Bromocyclopentanone**** (7.7 g) (b.p. 79-83° at 15 mm), 9 g of anhydrous potassium acetate and 20 g of glacial acetic acid were heated together on an oil bath at the boil for 2 hours. Water was added to the reaction mixture with cooling, followed by 26.5 g of sodium carbonate. The organic part was extracted with ether; the ethereal solution was washed with 10% sodium carbonate solution (until neutral) and dried with sodium sulfate. After the ether had been driven off, the residue distilled off nearly completely in vacuo (19 mm) at 98-102°, in agreement with data for α-acetoxycyclopentanone [4]. The Beilstein test gave a negative result.

Dibromocyclopentanone. The amounts of starting substances and the procedure were the same as for the preparation of monobromocyclopentanone. After it had been washed with sodium bicarbonate and dried, the ethereal solution of the bromination product was left in a crystallizer overnight. Much hydrogen bromide came off. The residue was a mixture of colorless crystals and a dark, viscous liquid. Alcohol was added to the mixture; the crystals were filtered and washed with alcohol; the colored impurities went completely into solution. After recrystallization from alcohol the m.p. was 68-69° and did not change after another recrystallization.

Found %: Br 65.88. $C_5H_6OBr_2$. Calculated %: Br 66.07.

Weight of dibromocyclopentanone 26.7 g (44.2%).

The reaction mixture resinified when we tried to convert the dibromo compound into the corresponding diacetoxy compound by heating with potassium acetate in a medium of glacial acetic acid. The same result followed attempts to prepare the product of addition of the dibromo compound with pyridine.

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* Distillation in a nitrogen stream gave the same result.

** After the first portion of cyclopentanone had been added, it was necessary to stir the mixture for a long period before reaction set in; otherwise the addition of a fresh portion of ketone might have led to excessively violent reaction.

*** The second fraction is evidently a mixture of products of decomposition of the dibromo compound. Special experiments with the crystalline dibromo compound showed that distillation at 6 mm results in breakdown to liquids whose boiling point is slightly higher than that of monobromocyclopentanone.

**** The bromocyclopentanone had to be reacted immediately after preparation in order to avoid resinification.

SUMMARY

1. Bromination of cyclohexanone with dioxane dibromide in a mixture of dioxane and absolute ether gives dibromocyclohexanone in 59-69% yield.

2. Bromination of cyclopentanone with dioxane dibromide under the same conditions also leads to the dibromo derivative as the main product; yield 44%; this compound is not described in the literature. At the same time monobromocyclopentanone is formed in a yield of about 36%. The monobromo compound is converted to α-acetoxycyclopentanone on heating with potassium acetate in a medium of glacial acetic acid.

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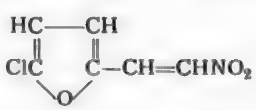
*Original Russian pagination. See C.B. Translation.

5-CHLOROFURYLNITROOLEFINS

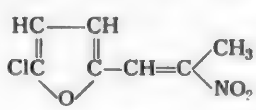
Z. N. Nazarova and F. T. Pozharskii

It was previously shown [1, 2] that halofurfurals containing bromine and iodine in the 5 position of the furan ring readily condense with nitroparaffins. In continuation of this work we now report on the products of condensation of 5-chlorofurfural with nitroparaffins. The literature contains quite a large number of syntheses on the basis of 5-chlorofurfural [3], but its condensation with nitroparaffins has not been studied. In recent years years papers and patents have been published on the application of nitroolefins of the aromatic and furan series as insectofungicides [4]. Introduction of a halogen atom into the furan ring stabilizes the latter and enhances the bactericidal activity of the resulting products [1, 5]. For these reasons we should expect the products of condensation of 5-chlorofurfural with nitroparaffins to be of practical interest.

We carried out the condensation of 5-chlorofurfural with nitromethane and nitroethane under various conditions. By a slight modification of the procedure of Moldenhauer [6] we succeeded in preparing 5-chlorofurylnitroethylene (I) in 86% yield. We prepared 5-chlorofurylnitropropene (II) in 79% by the method cited in [1].



(I)



(II)

5-Chlorofurylnitroolefins form light-yellow needles (from alcohol), insoluble in water, soluble in organic solvents, distillable in steam. In the same manner as the halogen in 5-bromo- and 5-iodo derivatives of furan, the chlorine in 5-chlorofurylnitroethylene and 5-chlorofurylnitropropene can be determined by the previously described procedure [2]. It has not yet been possible, however, to replace the chlorine by iodine or the nitro group as is possible with the bromine in 5-bromofurylnitroethylene [1, 2].

The 5-chlorofurylnitroolefins that we prepared exercise an irritant action on the mucous membrane of the nose.

EXPERIMENTAL

5-Chlorofurylnitroethylene. To a solution (cooled to -12°) of 3.2 g of sodium hydroxide in 16 ml of water and 4 ml of methanol was slowly added (dropwise) 2.81 g of nitromethane. The precipitated sodium salt of nitromethane was put for 10 minutes in a mixture of ice and salt and then completely dissolved by addition of 50 ml of ice water. The solution of the sodium salt of nitromethane was cooled to − 10° and dropwise addition was made, with vigorous stirring, of 5.22 g of 5-chlorofurfural [7] in 12 ml of methanol. After 10-minutes' stirring, the cold (− 10°), transparent solution of the sodium salt of chlorofurylnitroethanol was slowly run with frequent shaking into a cooled (− 5°) solution of 5 ml of concentrated sulfuric acid in 40 ml of water. The lemon-yellow precipitate of 5-chlorofurylnitroethylene was collected after standing for 20 minutes in the cold, thoroughly washed with cold water, and dried in a desiccator over sulfuric acid. Yield 5.98 g (86%), m.p. 103-104°; recrystallization from alcohol gave yellow plates with m.p. 105-106°.

Found %: Cl 20.35. $C_6H_4O_3NCl$. Calculated %: Cl 20.43.

Chlorofurylnitropropene. To a solution (cooled to $-10°$) of 1.305 g of 5-chlorofurfural and 1 g of nitroethane in 7.5 ml of methanol was added (dropwise with vigorous stirring) 0.6 g of sodium hydroxide in 4 ml of water. A small precipitate appeared after stirring 20 minutes and was completely dissolved by addition of 5 ml of ice water. The cold solution of the sodium salt of 5-chlorofurylnitropropanol was added dropwise with intensive shaking to 3.7 ml of 10% hydrochloric acid cooled to $-7°$. After 20-minutes' stirring of the mixture (cooled with ice and salt), light-yellow 5-chlorofurylnitropropene was deposited. The filtered product was dried in a desiccator over sulfuric acid and had m.p. 70-72°. Yield 1.485 g (79%). Recrystallization from alcohol gave light-yellow needles with m.p. 74-75°.

Found %: Cl 19.02. $C_7H_6O_3NCl$. Calculated %: Cl 18.90.

SUMMARY

Condensation of 5-chlorofurfural with nitromethane and nitroethane gave the previously undescribed 5-chlorofurylnitroethylene and 5-chlorofurylnitropropene in yields of 86 and 79% respectively.

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SYNTHESIS OF THIAZOLIDONE DERIVATIVES OF BIOLOGICAL INTEREST

IX. SYNTHESIS OF 3-DERIVATIVES OF 2,4-THIAZOLIDINEDIONE HYDRAZONE

E. V. Vladzimirskaia

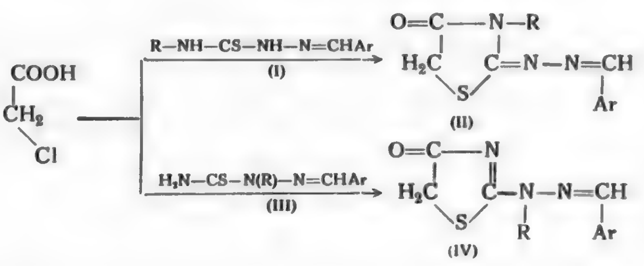
We previously [1] described the synthesis of p-acetaminobenzylidene hydrazones of 2,4-thiazolidinedione and of its 5-derivatives. The molecules of the products contain a hydrogen atom in the 3-position of the thiazolidine ring.

We aimed at synthesizing the 3-derivatives, for which purpose it was necessary to start from 4-derivatives of thibone* R

$$-\overset{4}{N}H-\overset{3}{C}S-\overset{2}{N}H-\overset{1}{N}=CH-C_6H_4-NHCOCH_3$$

and monochloroacetic acid. 4-Derivatives of "thibone" have not been described in the literature, nor have the corresponding products of their condensation with monochloroacetic acid. The introduction of alkyl or aryl substituents into the molecules of therapeutic agents is , however, often accompanied by considerable enhancement of physiological activity.

We prepared 4-methylthiosemicarbazide, 4-allylthiosemicarbazide and 4-phenylthiosemicarbazide by the method of Pulvermacher [2, 3] and condensed them in alcoholic solution with p-acetaminobenzaldehyde to give the corresponding "thibone" derivatives (I, Ar = $CH_3CONHC_6H_4$). The latter substances easily interact with monochloroacetic acid (see equation below) with formation of derivatives of 2,4-thiazolidinedione 2-hydrazone (II).



The 3-derivatives of 2,4-thiazolidinedione p-acetamino-2-benzylidenehydrazone that we synthesized are neutral substances, soluble in alkali solution only with difficulty at the boil.

In order to study the change of properties of preparations on transition from the thiazolidine ring to the thiazoline ring, we prepared benzaldehyde 2-phenylthiosemicarbazone (III, R = Ar = C_6H_5) by Pellizzari's method [4] and condensed it with monochloroacetic acid (see equation above). For purposes of comparison we also

* p-Acetaminobenzaldehyde thiosemicarbazone.

synthesized and examined the behavior of benzaldehyde thiosemicarbazone, benzaldehyde 4-phenylthiosemicarbazone, 2,4-thiazolidinedione 2-benzaldehydehydrazone, and also 3-phenyl-2,4-thiazolidinedione 2-benzylidenehydrazone (II, R = Ar = C_6H_5). The latter substance has not previously been described.

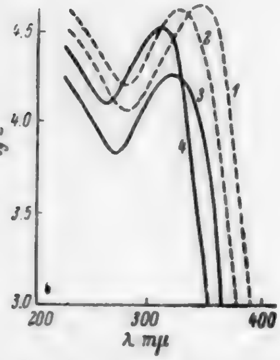


Fig. 1. 1) p-Acetaminobenzaldehyde 4-phenylthiosemicarbazone 2) 3-phenyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) benzaldehyde 4-phenylthiosemicarbazone, 4) Δ^2-4-thiazolinone 2-benzylidenephenylhydrazone.

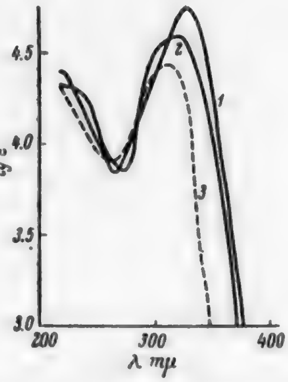


Fig. 2. 1) p-Acetaminobenzaldehyde 4-methylthiosemicarbazone 2) 3-methyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) 2,4-thiazolidinedione 2-benzylidenehydrazone.

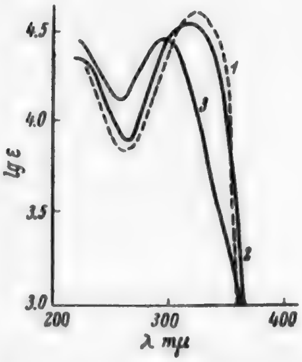


Fig. 3. 1) p-Acetaminobenzaldehyde 4-allylthiosemicarbazone, 2) 3-allyl-2,4-thiazolidinedione p-acetaminobenzylidene-2-hydrazone, 3) benzaldehyde thiosemicarbazone.

The ultraviolet absorption spectra of 4-derivatives of thibone scarcely differ from the corresponding spectra of thibone [5], and only in the case of the phenyl derivative do we observe a slight shift of the characteristic maximum and minimum and also of the long-wave edge of the curve (at ϵ 1000) in the long-wave direction. The diagram (Figs. 1-3) show that the absorption maxima of these substances are in the 330-337 mμ region and the minima in the 268-275 mμ region. The long-wave edge of the curves for ϵ 1000 is in the 365-375 mμ region. The absorption spectra of benzaldehyde thiosemicarbazone are very similar to the spectra of thibone and its derivatives but the p-acetamino group displaces the spectra slightly towards the longer waves. The introduction of the phenyl group into the benzaldehyde thiosemicarbazone molecule (Fig. 1) also has no appreciable influence on the change of form of the absorption curves. Since unsubstituted thiosemicarbazide lacks a characteristic maximum [5] in the 310-340 mμ region, the presence of such a maximum in the products of its condensation with aromatic aldehydes is associated with a direct influence of arylidene grouping on the C–S group.

Formation of a thiazolidione or thiazoline ring has no great influence on the absorption spectra in the ultraviolet both in respect of the principal maxima and of the intensity of absorption. At the same time we observe a slight shift of the maxima towards the shorter waves. These investigations show that contrary to our earlier suggestions [5] the study of the ultraviolet absorption spectra cannot solve the problem of the existence of tautomerism in the thiazolidone and thiazolinone rings. The problem of the structure of these rings will have to be solved by chemical and physicochemical methods, and perhaps also by investigations of absorption spectra at other wavelengths.

EXPERIMENTAL

Synthesis of 4-derivatives of p-acetaminobenzaldehyde thiosemicarbazone. 0.1 mole of 4-phenyl thiosemicarbazide was dissolved in alcohol at the boil and poured into a boiling alcoholic solution of 0.1 mole of p-acetaminobenzaldehyde. The mixture was refluxed for 2 hours. The reaction product, isolated from the reaction mixture after cooling, was filtered and recrystallized from alcohol. The prepared compounds are listed in Table 1.

Synthesis of derivatives of 2,4-thiazolidinedione 2-hydrazone. 5 mmol of the 4-derivative of p-acetaminobenzaldehyde thiosemicarbazone, 5 mmol of monochloroacetic acid and 0.8 g of anhydrous sodium

acetate were dissolved in 20-35 ml of glacial acetic acid and refluxed for 2 hours. The resulting transparent solution was diluted (after cooling) with an aqueous solution of sodium acetate. The reaction product was filtered and recrystallized from alcohol. The prepared substances are listed in Table 2.

TABLE 1

4-Derivatives of p-Acetaminobenzaldehyde Thiosemicarbazone

Preparation No.	Structure	Yield (in %)	Melting point	Nitrogen content (%)	
				found	calc.
1	(I), $R = CH_3$	30	237°	22.29	22.38
2	(I), $R = C_3H_5$	45	223—224	20.65	20.28
3	(I), $R = C_6H_5$	48	211	17.76	17.94

Similarly we synthesized 3-phenyl-2,4-thiazolidinedione 2-benzylidenehydrazone from benzaldehyde 4-phenylthiosemicarbazone, and also Δ^2-4-thiazolinone 2-benzylidenephenylhydrazone from benzaldehyde 2-phenylthiosemicarbazone. 2,4-Thiazolidinedione 2-benzylidenehydrazone (II, R = H, Ar = C_6H_5) was prepared by the method of Chabrier and Cattelain [6] by condensation of monochloroacetic acid with benzaldehyde thiosemicarbazone.

TABLE 2

Derivatives of Thiazolidone and Thiazoline

Preparation No.	Structure	Yield (in %)	Melting point	Analysis (%)	
				found	calc.
1	(II), $R = CH_3$, $Ar = CH_3CONHC_6H_4$	48	228°	C 53.63, H 5.02, N 19.30	C 53.67, H 4.86, N 19.30
2	(II), $R = C_3H_5$, $Ar = CH_3CONHC_6H_4$	76	187	C 56.90, H 5.30, N 17.97	C 56.94, H 5.10, N 17.71
3	(II), $R = C_6H_5$, $Ar = CH_3CONHC_6H_4$	55	270	N 16.12	N 15.90
4	(IV), $R = Ar = C_6H_5$	86	188—189	C 65.99, H 4.49, N 14.36	C 65.06, H 4.44, N 14.23
5	(II), $R = Ar = C_6H_5$	98	224	N 13.89	N 14.23

We carried out the spectrophotometric studies with the help of the SF-4 quartz spectrograph. Solutions of 1-2 mg/100 ml of solvent (ethanol) were prepared.

It is our duty to express thanks to N. M. Turkevich for valuable guidance during the present investigation.

SUMMARY

1. 3-Derivatives of 2,4-thiazolidinedione 2-arylidenehydrazones were prepared for the first time.

2. It was established that the ultraviolet absorption spectra of 2'-arylidene derivatives of 2,4-thiazolidinedione 2-hydrazone, both substituted and unsubstituted in the 3-position, do not differ appreciably from the spectra of the original thiosemicarbazones.

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INTERACTION OF β-CHLOROVINYL KETONES WITH β-DICARBONYL COMPOUNDS

V. KETOVINYLATION OF α-ALKYL ACETOACETIC ESTERS

N. K. Kochetkov, B. P. Gottikh and L. I. Kudriashov

In preceding communications it was shown that β-chlorovinyl ketones react smoothly with metal derivatives of alkylmalonic [1] and malonic [2] esters with formation of normal products of ketovinylation – γ-ketoalkenyl malonic esters. Since transformations of this new class of substances opened out a route to previously inaccessible types of organic compounds [2, 3], it seemed of interest to broaden the scope of the ketovinylation of compounds with a mobile methylene and methine chain. In the first instance we studied the ketovinylation of α-alkyl acetoacetic esters and now present our results.

Previously we studied the interaction of β-chlorovinyl ketones with acetoacetic ester in presence of potassium carbonate in boiling toluene [4] which showed that the process is complicated by subsequent transformations of the primary products of ketovinylation to give derivatives of alkylsalicylic acids and compounds of unknown structure formed by interaction of two molecules of β-chlorovinyl ketone with one molecule of acetoacetic ester. α-Alkylacetoacetic esters contain only one labile hydrogen atom; such secondary processes are therefore ruled out in the present case, and we should expect formation of only products of normal ketovinylation.

In fact, reaction of β-chlorovinyl ketones with sodium derivatives of α-alkylacetoacetic esters in benzene under conditions similar to those that we described for the ketovinylation of alkylmalonic esters [1] lead smoothly and in good yields to the previously unknown α-alkyl-α-(γ-ketoalkenyl)-acetoacetic esters.

$$\mathrm{RCOCH{=}CHCl + CH_3COCHR'COOC_2H_5 \longrightarrow RCOCH{=}CH\underset{\displaystyle COCH_3}{\overset{\displaystyle R'}{\overset{|}{\underset{|}{C}}}}{-}COOC_2H_5}$$

$$\mathrm{R = CH_3,\ C_2H_5,\ C_3H_7.} \qquad \mathrm{R' = C_2H_5,\ C_4H_9.}$$

Due to the accessibility of the starting substances and the simplicity of operation, the method that we developed is an extremely convenient one for the preparation of this class of compounds which is of interest and promise for synthetic chemistry.

The prepared compounds are high-boiling oils, stable in storage but easily resinifying on distillation in a too-low vacuum. Their purification must therefore be effected with suitable precautions (see Experimental).

The structures of the prepared compounds are confirmed by analyses. Hydrogenation of one of the compounds – ethyl-(3-ketobutenyl-1)-acetoacetic ester – indicates the presence of one double bond in the products of ketovinylation. An alternative possibility of ketovinylation at the oxygen (by analogy with known cases of acylation of acetoacetic esters with acid chlorides) must be rejected since the products that we prepared are stable towards mineral acids under mild conditions, whereas it is well known that β-substituted vinyl ketones of the type of RCOCH=CH-X, where X = OR, OAr (for example phenoxyvinyl ketones and alkoxyvinyl ketones) are easily hydrolyzed under such conditions, the ketovinyl residue being split off with formation of a symmetrical triacyl benzene (for example [5]). Moreover, the structure of the prepared compounds is confirmed by some of their transformations which we shall report on in later communications.

EXPERIMENTAL

Ethyl-(3-ketobutenyl-1)-acetoacetic ester. 7.5 g of sodium finely dispersed in xylene and 300 ml of dry benzene were placed in a three-necked flask fitted with stirrer, reflux condenser and dropping funnel; dropwise addition of 54 g of ethyl acetoacetic ester with stirring was then made. The reaction mixture was slowly heated on a water bath; after the whole of the ethyl acetoacetic ester had been added, the mixture was boiled until the whole of the sodium had gone into solution (2-3 hours). It was then cooled with ice water. A solution of 30 g of methyl β-chlorovinyl ketone in 75 ml of dry benzene was then added dropwise (vigorous stirring) in the course of 1-1.5 hours. (A flask of adequate size must be used because considerable foaming occurs during the addition of the ketone.) After the whole of the ketone had been added, the cooling was stopped and the reaction mixture boiled for 2.5-3 hours and then washed with water (2 × 100 ml). The wash waters were extracted with ether and the ether extracts were combined with the benzene solution. The combined ether-benzene extracts were dried with sodium sulfate, the solvents were driven off and the residue distilled in vacuo. The fraction boiling at 130-145° (5 mm) was collected.*

After 3 distillations the compound had the following constants: b.p. 108-110° (1 mm), d_4^{20} 1.0550, n_D^{20} 1.4670, MR_D 59.51; calculated 56.92. Yield 42.0 g (64.5%).

Found %: C 63.91, 63.81; H 8.07, 8.12. $C_{11}H_{16}O_4$. Calculated %: C 63.71; H 8.02.

Ethyl-(3-ketobutenyl-1)-acetoacetic ester is a colorless oil with a characteristic odor, miscible with organic solvents, insoluble in water. It has a long duration of stability.

Ethyl-(3-ketopenten-1-yl-1)-acetoacetic ester is similarly prepared from 7 g of sodium, 52 g of ethylacetoacetic ester and 36 g of ethyl β-chlorovinyl ketone in 330 ml of dry benzene. The fraction with b.p. 128-135° (3 mm) was collected.

After 3 distillations the substance had the following constants: b.p. 115-117° (1 mm), d_4^{20} 1.0415, n_D^{20} 1.4665, MR_D 64.01; calculated 63.44. Yield 43.5 g (52%).

Found %: C 65.32, 65.20; H 7.99, 8.05. $C_{12}H_{20}O_4$. Calculated %: C 64.97; H 8.39.

Ethyl-(3-ketohexen-1-yl-1)-acetoacetic ester was prepared from 6 g of sodium, 43 g of ethyl acetoacetic ester and 31 g of propyl β-chlorovinyl ketone in 300 ml of dry benzene. The fraction with b.p. 151-160° (5 mm) was collected.

After 3 distillations the compound had the following constants: b.p. 120-122° (1 mm), d_4^{20} 1.0270, n_D^{20} 1.4657, MR_D 68.53; calculated 68.03. Yield 42 g (72%).

Found %: C 66.02, 65.89; H 8.53, 8.56. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72.

n-Butyl-(3-ketobutenyl-1)-acetoacetic ester was prepared from 4.8 g of sodium, 44.6 g of n-butylaceto-acetic ester and 20.9 g of methyl β-chlorovinyl ketone in 200 ml of dry benzene. The fraction with b.p. 153-164° (6 mm) was collected.

After 3 distillations the compound had the following constants: b.p. 139-140° (2 mm), d_4^{20} 1.0274, n_D^{20} 1.4662, MR_D 68.58; calculated 68.06. Yield 27.9 g (55%).

Found %: C 65.98, 66.13; H 8.77, 8.90. $C_{14}H_{22}O_4$. Calculated %: C 66.12; H 8.72.

n-Butyl-(3-ketohexen-1-yl-1)-acetoacetic ester was prepared from 3 g of sodium, 26 g of n-butylacetoacetic ester and 15 g of propyl β-chlorovinyl ketone in 150 ml of dry benzene. On distillation in vacuo the fraction with b.p. 137-145° (2 mm) was collected.

After 3 distillations in vacuo the compound had: b. p. 137-138° (1 mm), d_4^{20} 1.0007, n_D^{20} 1.4650, MR_D 78.19; calculated 77.30. Yield 24 g (75%).

* Distillation is best effected from a Claisen flask without a column and with a low side-tube. At first it is necessary to distill the substance rapidly with addition of hydroquinone and preferably in a current of inert gas. This enables the yield to be raised by 10-15%.

Found %: C 68.30, 68.56; H 9.48, 9.40. $C_{16}H_{26}O_4$. Calculated %: C 68.06; H 9.28.

Hydrogenation of ethyl-(3-ketobutenyl-1)-acetoacetic ester. 28.5 g of ethyl-(3-ketobutenyl-1)-acetoacetic ester was hydrogenated in 100 ml of ether over palladium deposited on barium sulfate. After 3045 ml of hydrogen (0°, 760mm) had been absorbed, hydrogenation was stopped (the theoretical requirement was 3070 ml of hydrogen). The catalyst was filtered off, the ether was distilled off, and the residue was distilled in vacuo. The fraction with b.p. 115-117° (3 mm) was collected.

After 3 distillations the substance had: b.p. 104-105° (1 mm), d_4^{20} 1.0429, n_D^{20} 1.4500, MR_D 58.84; calculated 59.29. Yield 28.0 g (quantitative).

Found %: C 63.45; H 8.87. $C_{12}H_{20}O_4$. Calculated %: C 63.13; H 8.83.

Ethyl-(3-ketobutyl)-acetoacetic ester is a colorless oil, miscible with organic solvents, insoluble in water, and stable in storage.

SUMMARY

The interaction of β-chlorovinyl ketones with α-alkylacetoacetic esters was studied. The products are α-alkyl-α-(γ-ketoalkenyl)-acetoacetic esters. The reaction is a convenient means of synthesis of compounds of this new class (yield 50-75%).

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INTERACTION OF β-CHLOROVINYL KETONES WITH

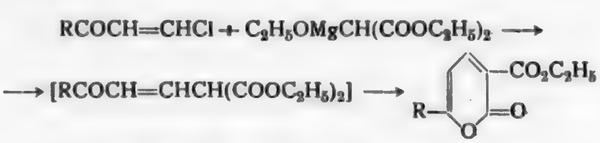
β-DICARBONYL COMPOUNDS

VI SYNTHESIS OF SOME DERIVATIVES OF α-PYRONES

N. K. Kochetkov and L. I. Kudriashov

In the preceding communications [1, 2] we described the ketovinylation of malonic and alkylmalonic esters. Interaction of ethoxymagnesium malonic ester with β-chlorovinyl ketones led to formation of γ-ketoalkenylmalonic esters, which underwent cyclization under the action of acetyl chloride or certain acidic reagents and formed 6-alkyl-3-carbethoxy-α-pyrones [2]. This new route to α-pyrones has, however, defects associated with certain experimental difficulties during the synthesis and isolation of γ-ketoalkenylmalonic esters, as well as with the conditions of cyclization. The latter leads to severe resinification of the reaction mixture if the γ-ketoalkenylmalonic ester is not previously purified.

We recently developed a new and more convenient variant of the synthesis of α-pyrones which may be described briefly as follows: A toluene solution of the β-chlorovinyl ketone was added to ethoxymagnesium malonic ester prepared in the minimum quantity of alcohol; after the reaction was completed by heating the perfectly homogeneous mixture is decomposed with glacial acetic acid, and the resulting γ-ketoalkenylmalonic ester (without purification) is cyclized to the α-pyrone by heating with acetic anhydride or acetyl chloride (the latter gives slightly better results).



$R = C_3H_7,\ C_5H_{11},\ C_7H_{15},\ C_6H_5.$

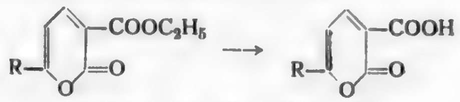
A careful investigation of the reaction mixture, carried out during synthesis of the propyl homolog, showed that a very small quantity (0.5-1%) of a substance with m. p. 104-104.5° (not a pyrone) is formed at the same time as the pyrone under the reaction conditions. Analysis and determination of molecular weight of the product of saponification indicated the formula $C_{17}H_{20}O_4$. Its structure was not investigated; however, it evidently contains an aromatic ring since treatment with nitration mixture readily gives a nitro derivative containing an aromatic group. Similar secondary products are evidently also formed during synthesis of other homologs; in all cases, however, they are formed in such small quantity that they do not hinder to the slightest degree the separation of the pyrone, and they do not detract from the proposed value of our method of synthesis.

The new procedure thus makes superfluous the isolation of γ-ketoalkenyl malonic esters in the pure form; this considerably simplifies the whole synthesis which is essentially a direct synthesis of derivatives of α-pyrone (in yields of about 40%) from β-chlorovinyl ketones.

By this method we prepared 6-phenyl-, 6-propyl-, 6-amyl- and 6-heptyl-3-carbethoxy-α-pyrones. The two last substances have not previously been described.

The new method makes 6-alkyl-3-carbethoxy-α-pyrones easily accessible substances; on their basis we were therefore able to prepare several derivatives of that type with the objective of throwing light upon the

physiological activity of derivatives of α-pyrone. No information on this question has appeared in the literature, although the high physiological activity of derivatives of corresponding condensed systems – coumarin and chromone* is well-known. With this objective we first studied the possibility of preparing derivatives of 6-alkyl-α-pyrone-3-carboxylic acids. Hydrolysis of the prepared 6-alkyl-3-carbethoxy-α-pyrones is easily effected by heating them with concentrated hydrochloric acid (yield about 70%).



$R = CH_3, C_3H_7, C_5H_{11}, C_7H_{15}, C_6H_5$.

This ease of hydrolysis depends on the nature of the substituent in the 6-position. Thus, hydrolysis of 6-methyl-3-carbethoxy-α-pyrone requires a half-hour's heating with concentrated hydrochloric acid at 60°; the heptyl homolog ($R = C_7H_{15}$) is saponified by one-and-a-half-hour's heating at 70°, while the phenyl homolog ($R = C_6H_5$) already requires boiling for one and a half hours with concentrated hydrochloric acid. It should be noted that 6-alkyl-3-carbethoxy-α-pyrones can also be hydrolyzed with concentrated hydrochloric acid at room temperature, but the operation is then a very lengthy one.

The resulting 6-substituted α-pyronecarboxylic acids are colorless, crystalline substances, differing from one another in their behavior on heating. Thus, 6-methyl-α-pyrone-3-carboxylic acid undergoes decarboxylation on melting or on heating in solution at above 70°; its aliphatic analogs withstand heating in solutions to 100°, while 6-phenyl-α-pyrone-3-carboxylic acid can even be distilled unchanged in vacuo.

An attempt to prepare substituted amides of these acids by the direct action of amines on substituted 3-carbethoxy-α-pyrones was unsuccessful, because the reaction is then directed towards cleavage of the pyrone ring (this behavior will be the subject of a later communication). The preparation of compounds of the type in question, which we carried out in the case of 6-methyl-α-pyrone-3-carboxylic acid, could only be realized via the corresponding acid chloride. The latter was obtained by the action of thionyl chloride on the corresponding acid. Treatment of the acid chloride with aniline and diethylamine gave the anilide and diethylamide of 6-methyl-α-pyrone-3-carboxylic acid. Treatment of the acid chloride with hydrazine gave only N,N'-bis-(6-methyl-α-pyronyl-3)-hydrazine, and a monosubstituted hydrazide could not be isolated. Futher investigation of the acid chlorides of α-pyronecarboxylic acids led to the preparation of a wide range of the corresponding derivatives. All of the prepared compounds were subjected to pharmacological tests, the results of which will be communicated separately.

EXPERIMENTAL

6-Propyl-3-carbethoxy-α-pyrone. 6 g of magnesium was put into a three-necked flask fitted with stirrer, dropping funnel and reflux condenser (a calcium chloride tube topped the latter); the magnesium was activated by heating with a crystal of iodine. Dropwise addition was then made of a mixture of 35 ml of malonic ester and 10 ml of anhydrous alcohol. After the violent reaction had subsided, another mixture of 10 ml of malonic ester and 25 ml of anhydrous alcohol was added and the mass was boiled until the whole of the magnesium had dissolved (about 2 hours); it was then cooled in an ice bath, and dropwise addition was made (vigorous stirring) in the course of an hour of a solution of 26.5 g of propyl β-chlorovinyl ketone in 20 ml of anhydrous toluene. In some cases a precipitate of ethoxymagnesium malonic ester came down on cooling and the stirring was stopped. In such cases the reaction was started without stirring, but after introduction of only about one-fifth of the total quantity of ketone, the reaction mixture became sufficiently dilute to permit stirring. After the propyl β-chlorovinyl ketone had been added, the reaction mass was stirred for 30 minutes at room temperature and then heated for 1.5 hours on a boiling water bath. After cooling, 40 ml of glacial acetic acid was added, followed by 100 ml of water (the aqueous layer must have a weakly acidic reaction to litmus), and the resulting oil was extracted with toluene (3 × 30 ml). The toluene was distilled off; the thermometer in the liquid registered 140° at the end of the distillation. 100 ml of acetyl chloride was added to the residue and the mixture was boiled for 4 hours. After cooling, the acetyl chloride was added to the residue and the mixture was boiled for 4 hours. After cooling, the acetyl chloride was distilled off; the residue was then distilled, the 154-192° (3-5 mm) fraction being collected (28.0 g). Distillation with glass wool is recommended in view of the considerable decomposition during the operation. Redistillation gave 18.1 g (43%) of 6-propyl-3-carbethoxy-α-pyrone.

B.p. 145-148° (1 mm), d_4^{20} 1.1285, n_D^{20} 1.5170 (the erroneous value of 1.5770 was previously reported [1]).

Found %: C 62.88, 62.95. H 6.79, 6.84. $C_{11}H_{14}O_4$. Calculated %: C 62.84; H 6.71.

A white crystalline substance with m. p. 104-104.5° (from alcohol) came down after 3-5 days from the higher fractions after separation of the 6-propyl-3-carbethoxy-α-pyrone.

Found %: C 71.17, 71.05; H 7.22, 7.29. $C_{17}H_{20}O_4$. Calculated %: C 70.81; H 6.99.

6-Amyl-3-carbethoxy-α-pyrone. Prepared under the same conditions (see preceding experiment) from 6 g of magnesium, 45 ml of malonic ester and 32.1 g of amyl β-chlorovinyl ketone, with 35 ml of anhydrous alcohol and 100 ml of acetyl chloride. The 159-194° (2-4 mm) fraction (33.1 g) was collected on distillation. A redistillation gave 21.3 g (44%) of 6-amyl-3-carbethoxy-α-pyrone.

B.p. 147-150° (0.5 mm), 165-166° (1 mm), d_4^{20} 1.0994, n_D^{20} 1.5128.

Found %: C 65.49, 65.58; H 7.67, 7.60. $C_{13}H_{18}O_4$. Calculated %: C 65.53; H 7.62.

6-Heptyl-3-carbethoxy-α-pyrone. Similarly prepared from 3 g of magnesium, 23 ml of malonic ester and 18.85 g of heptyl β-chlorovinyl ketone, using 17 ml of alcohol and 50 ml of acetyl chloride. The fraction with b.p. 173-198° (2-4 mm) was collected on distillation (16.4 g). Redistillation gave 10.2 g (38.3%) of 6-heptyl-3-carbethoxy-α-pyrone.

B.p. 159-162° (0.5 mm). After redistillation b.p. 161-162° (0.5 mm), d_4^{20} 1.0555, n_D^{20} 1.5079.

Found %: C 67.83, 67.71; H 8.69, 8.48. $C_{15}H_{22}O_4$. Calculated %: C 67.64; H 8.33.

6-Phenyl-3-carbethoxy-α-pyrone. Similarly prepared from 1.9 g of magnesium, 16 ml of malonic ester and 9.7 g of phenyl β-chlorovinyl ketone, with use of 8 ml of alcohol and 25 ml of acetyl chloride. After the acetyl chloride had been removed from the reaction mixture, the fraction coming off up to 110° (6 mm) was taken off in vacuo; the residue was dissolved in a little methanol, and 6-phenyl-3-carbethoxy-α-pyrone was brought down with water. Yield 7.7 g (55%), m.p. 105° (from methanol) [3].

6-Alkyl-α-pyrone-3-carboxylic acids. 0.91 mole of 6-alkyl-3-carbethoxy-α-pyrone was heated with 5.5 ml of concentrated hydrochloric acid (50 ml in the case of the phenyl homolog); after cooling, the mass was diluted with 4 times the quantity of water, dried in vacuo over phosphorus pentoxide and recrystallized. Reaction conditions and properties of the pyronecarboxylic acids are presented in the table.

6-Alkyl-α-pyrone-3-carboxylic Acids

R	Period of heating and temperature	Yield (in %)	Melting point	Solvent for recrystallization	Found (%) C	Found (%) H	Calculated (%) C	Calculated (%) H
CH_3	30 min. 60—64°	70.0	163—164° (разл.)	Dioxane, 80°	54.71, 54.84	4.05, 3.99	54.55	3.92
C_3H_7	30 min. 70	74.6	113	Alcohol	59.38, 59.54	5.48, 5.51	59.34	5.53
C_5H_{11}	75 min. 70	76.2	120—121	Alcohol	62.86 62.76	6.70, 6.72	62.84	6.71
C_7H_{15}	120 min. 70	58.2	119—120	Alcohol	65.55, 65.66	7.76, 7.78	65.53	7.62
C_6H_5	90 min., boiling	77.0	170—171**	Glacial acetic acid	66.81, 66.62.	3.88, 3.84	66.67	3.73

Anilide of 6-methyl-α-pyrone-3-carboxylic acid. 0.4 g of 6-methyl-α-pyrone-3-carboxylic acid and 6 ml of freshly distilled thionyl chloride were heated for 1 hour at 40°; the next day the product was evaporated in vacuo, the residue was dissolved in 10 ml of absolute ether, and 0.5 g of aniline in 5 ml of absolute ether was added dropwise to the solution. After 30 minutes the aniline hydrochloride was filtered off, the ethereal solution was evaporated, and the anilide of 6-methyl-α-pyronecarboxylic acid was obtained. Yield 0.32 g (53%), m. p. 146° (from aqueous alcohol).

Found %: N 5.97, 6.38. $C_{13}H_{11}O_3N$. Calculated %: N 6.11.

6-Methyl-α-pyrone-3-carboxylic acid chloride. 4.8 g of 6-methyl-α-pyrone-3-carboxylic acid and 7 ml of freshly distilled thionyl chloride were heated for 6 hours at 40-50°; the solid, crystalline mass was recrystallized from 13 ml of anhydrous benzene, washed with 2 ml of anhydrous benzene, and dried in vacuo over paraffin wax. Yield of 6-methyl-α-pyrone-3-carboxylic acid chloride 4.6 g (86.8%), m.p. 127-127.5° (from benzene).

Found %: Cl 20.28, 20.35. $C_7H_5O_3Cl$. Calculated %: Cl 20.55.

6-Methyl-α-pyrone-3-carboxylic acid diethylamide. A solution of 4.2 ml of diethylamine in 20 ml of absolute benzene was added with cooling to a solution of 3.5 g of 6-methyl-α-pyrone-3-carboxylic acid chloride in 60 ml of absolute ether. After 3 hours, the diethylamine hydrochloride was filtered off, the filtrate was evaporated, and the diethylamide of 6-methyl-α-pyronecarboxylic acid was isolated in a yield of 3.2 g (76.2%), m.p. 57-58° (from a mixture of benzene and ligroine).

Found %: C 62.85, 62.80; H 7.19, 7.17. $C_{11}H_{15}O_3N$. Calculated %: C 63.14; H 7.23.

N,N'-Bis-(6-methyl-α-pyronyl-3)-hydrazine. 2.2 ml of hydrazine hydrate was added dropwise with cooling and vigorous stirring to a solution of 3.5 g of 6-methyl-α-pyrone-3-carboxylic acid chloride in 80 ml of absolute benzene. After two hours the reaction mass was heated to the boil; after cooling, the precipitate of N,N'-bis-(6-methyl-α-pyronyl-3)-hydrazine was filtered off and washed twice with hot benzene in water. Yield 2.3 g (38%). After recrystallization from glacial acetic acid, a specimen did not melt on heating to 400°.

Found %: C 55.04, 55.14; H 3.98, 4.07. $C_{14}H_{12}O_6N_2$. Calculated %: C 55.26; H 3.98.

SUMMARY

1. A direct method was developed for the synthesis of 6-substituted 3-carbethoxy-α-pyrones by condensing β-chlorovinyl ketones with ethoxymagnesium malonic ester followed by cyclization of the reaction product by treatment with acetyl chloride (yield 40%).

2. The prepared 6-alkyl(aryl)-3-carbethoxy-α-pyrones were hydrolyzed to the corresponding acids by treatment with concentrated hydrochloric acid.

3. Some derivatives of 6-methyl-α-pyrone-3-carboxylic acid were prepared.

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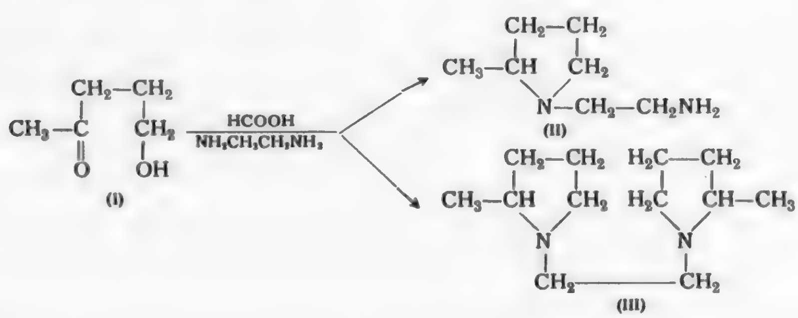
SYNTHESIS AND PROPERTIES OF PYRROLIDINE BASES

IV. 2-METHYL-N-β-AMINOETHYLPYRROLIDINE AND SOME OF ITS TRANSFORMATIONS

A. P. Terent'ev, M. A. Volodina and V. G. Mishina

In the preceding communications [1-3] we showed that γ-ketoalcohols are an accessible starting point for the preparation of pyrrolidine and pyrrolidone bases. Some of the compounds that we prepared in these series exhibited considerable physiological activity (tests were carried out in the Institute of Pharmacology of the Academy of Medical Sciences of the USSR). This prompted us to undertake the synthesis of 2-methyl-N-β-aminoethylpyrrolidine and to study some of its reactions. The present investigation was of interest from the viewpoint of synthesis of compounds with possible pharmacological activity.

By reaction of γ-acetopropyl alcohol (I) with N,N'-ethyleneformamide we obtained a 60% yield of 2-methyl-N-β-aminoethylpyrrolidine (II) together with 2,2-dimethyl-N,N'-dipyrrolidineethane (III). Preliminary tests of 2-methyl-N-β-aminoethylpyrrolidine indicated considerable physiological activity.

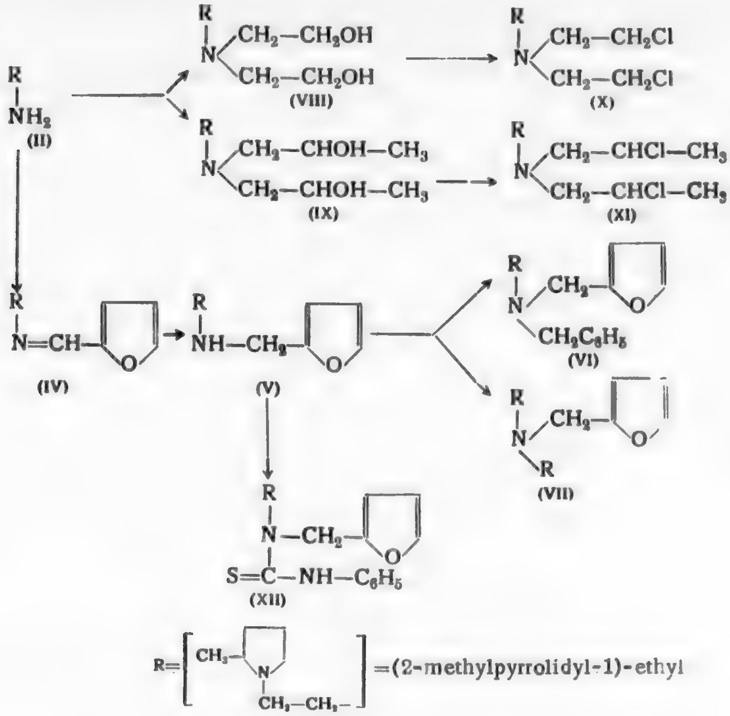


We studied some transformations of 2-methyl-N-β-aminoethylpyrrolidine (II). Its reaction with furfural gave 2-methyl-N-β-furylideneaminoethylpyrrolidine (IV), reduction of which by magnesium in methanol (Zechmeister's method [4]) gave 2-methyl-N-β-furylaminoethylpyrrolidine (V). We obtained the corresponding tertiary amines by reacting (V) with benzyl chloride and 2-methyl-β-chloroethylpyrrolidine: N-2-furyl-N-benzyl-β-(2-methylpyrrolidyl-1)-ethylamine (VI) and N-2-furyl-N-(2-methylpyrrolidyl-1-ethyl)-β-(2-methylpyrrolidyl-1)-ethylamine (VII).

Treatment of (V) with phenyl isocyanate gave N-phenyl-N'-2-(2-methyl-N-pyrrolidyl)-ethyl-N'-furylthiourea (XII).

Reaction of ethylene oxide and propylene oxide with (II) gave the amino alcohols N,N-β,β'-dihydroxydiethyl-β-(2-methylpyrrolidyl-1)-ethylamine (VIII) and N,N-β,β'-dihydroxydipropyl-β-(2-methylpyrrolidyl-1)-ethylamine (IX), which were subsequently converted to the corresponding β-chloroalkylamines: N,N-(β,β'-dichlorodiethyl)-β-(2-methylpyrrolidyl-1)-ethylamine (X) and N,N-(β,β'-dichlorodipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (XI).

All of the above-described transformations can be represented by the following scheme:



EXPERIMENTAL

We used commercial acetopropyl alcohol which was distilled in vacuo.

B. p. 114-115° (30 mm), n_D^{20} 1.4395, d_4^{20} 1.0068, MR_D 26.69. Literature data [5]: b. p. 115-116° (30 mm), n_D^{20} 1.4390.

2-Methyl-N-β-aminoethylpyrrolidine (II) and 2,2-dimethyldipyrrolidylethane (III). 40.8 g of γ-acetopropyl alcohol was heated with the formyl derivative of ethylenediamine (from 96 g of ethylenediamine) and 4 g of nickel powder for 20-25 hours at 130-180° (the temperature gradually rose with progressive weakening of the stream of evolved carbon dioxide). After cooling, the reaction mixture was hydrolyzed by boiling for 2 hours with 200 ml of concentrated hydrochloric acid and then neutralized with 40% sodium hydroxide solution until it had a strongly alkaline reaction. The reaction product was extracted with ether; the ethereal extracts were dried with fused alkali and fractionated. Yield 30 g (60.4%) of compounds (II).

B.p. 56-58° (8 mm), n_D^{20} 1.4640, d_4^{20} 0.88725, MR_D 39.87; calculated 39.67.

Dipicrate, m.p. 222-224°.

Found %: C 38.77, 38.69; H 3.88, 3.82. $C_{19}H_{22}O_{14}N_8$. Calculated %: C 38.93; H 3.78.

In addition to (II), 8 g (10%) of (III) was isolated.

B.p. 110-115° (8 mm), n_D^{20} 1.4730, d_4^{20} 0.90078, MR_D 61.20; calculated 61.14.

Dipicrate, m.p. 245-247°.

Found %: C 43.66, 43.71; H 4.75, 4.62. $C_{24}H_{30}O_{14}N_8$. Calculated %: C 44.19; H 4.62.

2-Methyl-N-(β-furylideneaminoethyl)-pyrrolidine (IV). Compound (IV) was prepared by the method described by Hansal [6] for N-furylidene-o-anisidine [6]. 12.8 g of compound (II) was mixed with 9.6 g of freshly distilled furfural. The mixture was left for 2 hours at room temperature and then held for 2 hours at 30-35°.

Distillation in vacuo gave 18 g (90%) of 2-methyl-N-β-furylideneaminoethylpyrrolidine.

B.p. 143-144° (4 mm), n_D^{20} 1.5250, d_4^{20} 1.0211, MR_D 62.27; calculated 61.97.

Dipicrate (from acetone), m. p. 245°.

Found %: C 43.25, 43.42; H 3.59, 3.57. $C_{24}H_{24}O_{15}N_8$. Calculated %: C 43.38; H 3.64.

2-Methyl-N-(β-furylaminoethyl)-pyrrolidine (V) Reduction of (IV) was performed by Zechmeister's [4] and Hansal's [7] methods, 13 g of compound (IV), 10.5 g of purified magnesium and 150 mg of anhydrous methyl alcohol were put into a two-necked flask fitted with a mechanical stirrer and a reflux condenser. After a short time the reaction commenced with considerable heat evolution and was completed in 15-20 minutes, the magnesium going completely into solution. The alcohol was distilled off; the residue was decomposed with ice and 40% acetic acid, made alkaline with 40% sodium hydroxide solution, and distilled with steam. The distillate was extracted with ether, and the extracts were dried with fused alkali and fractionated to give 4 g (30%) of 2-methyl-N-β-(N'-furylaminoethyl)-pyrrolidine (V).

B. p. 152-154° (15 mm), n_D^{20} 1.4910, d_4^{20} 0.9886, MR_D 61.02; calculated 61.46.

Dipicrate, m.p. 144-145° (from acetone and alcohol).

Found %: C 43.00, 43.15; H 4.33, 4.23. $C_{24}H_{26}O_{15}N_8$. Calculated %: C 43.24; H 3.93.

Heating of 1 g of (V) with 0.65 g of phenyl isothiocyanate resulted in formation of N-phenyl-N'-2-(2-methyl-N-pyrrolidyl)-ethyl-N'-furylthiourea (XII). Yield 86%, m. p. 90-91° (from alcohol).

Found %: C 66.26, 66.41; H 7.41, 7.37. $C_{19}H_{25}ON_3S$. Calculated %: C 66.44; H 7.33.

N-2-Furyl-N-benzyl-β-(2-methylpyrrolidyl-1)-ethylamine (VI). The method described in the literature for the preparation of tertiary pyrrolidylethylamines [8] was employed. A mixture of 5.2 g of (V), 5.3 g of anhydrous sodium carbonate and 6.3 g of benzyl chloride was heated on an oil bath at 160° for 6 hours. After the reaction mixture had cooled, 70 ml of water was run in and the solution was extracted with ether. The ethereal extracts were dried over fused caustic alkali. Two distillations gave 5.6 g (40%) of (VI).

B.p. 194-196° (10 mm), n_D^{20} 1.5365, d_4^{20} 1.0334, MR_D 90.11; calculated 90.46.

Dipicrate (from 50% acetic acid), m.p. 165-166°.

Found %: C 49.07, 49.32; H 4.00, 4.32. $C_{31}H_{32}O_{15}N_8$. Calculated %: C 49.20; H 4.10.

N-2-Furyl-N-(2-methyl-β-ethylpyrrolidyl-1-)-ethylamine (VII). Preparation was on the same lines as for (VI), starting from 5.2 g of (V), 5.3 g of anhydrous sodium carbonate and 7.4 g of 2-methyl-N-β-chloroethylpyrrolidine. 5.5 g (35%) of (VII) was obtained.

B.p. 182-183° (5 mm), n_D^{20} 1.4970, d_4^{20} 0.9777, MR_D 95.62; calculated 95.87.

Dipicrate (from 50% acetic acid), m.p. 133-135°.

Found %: C 47.73, 47.98; H 4.90, 5.20. $C_{31}H_{39}O_{15}N_9$. Calculated %: C 47.87; H 5.00.

N,N-β,β'-Dihydroxydiethyl-β-(2-methylpyrrolidyl-1)-ethylamine (VIII). 12.8 g of (II) was heated in an ampoule with 35.4 g of ethylene oxide in 150 ml of ethyl alcohol at 100° for 6 hours. The alcohol was taken off in vacuo and the residue was fractionated to give 18 g (83%) of (VIII).

B.p. 185-190° (10 mm), n_D^{20} 1.4885, d_4^{20} 1.0218, MR_D 61.05; calculated 61.70.

Dipicrate (from acetone), m.p. 167-168°.

Found %: C 41.77, 41.66; H 4.76, 4.87. $C_{23}H_{30}O_{16}N_8$. Calculated %: C 40.98; H 4.48.

N,N-(β,β'-dihydroxydipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (IX) was similarly prepared from 12.8 g of (II) and 46.4 g of propylene oxide. Yield 21 g (84%) of substance (IX).

B.p. 168-170° (2 mm), n_D^{20} 1.4770, d_4^{20} 0.98067, MR_D 70.40, calculated 70.90.

N,N-(β,β'-Dichlorodiethyl)-β-(2-methylpyrrolidyl-1)-ethylamine dihydrochloride (X). Into a three-necked flask fitted with mechanical stirrer were charged 9 g of (VIII) and 45 ml of chloroform. ml of thionyl chloride in 15 ml of chloroform was gradually added dropwise, after which the mixture was kept at 45° for 2 hours. After the excess of thionyl chloride and the chloroform had been removed in vacuo, 12 g of oil was isolated. The latter crystallized after standing for many days in a vacuum-desiccator. The crystals were boiled with carbon and recrystallized from anhydrous methanol to give 8 g (61%) of the dihydrochloride of (X). M.p. 198-200°.

Found %: C 40.78, 40.75; H 7.54, 7.68. $C_{11}H_{24}N_2Cl_4$. Calculated %: C 40.48; H 7.41.

N,N-(β,β' Dichlorodipropyl)-β-(2-methylpyrrolidyl-1)-ethylamine (XI) dihydrochloride. Prepared on the same lines as (X) from 12.5 g of (IX) and 9 ml of thionyl chloride. Yield 24 g of (XI) in the form of an oil which did not crystallize even on prolonged standing.

Found %: C 43.62, 43.75; H 7.62, 7.56. $C_{13}H_{28}N_2Cl_4$. Calculated %: C 44.10; H 7.97.

SUMMARY

Heating of a mixture of γ-acetopropyl alcohol and monoformylethylenediamine in presence of nickel gave 2-methyl-N-β-aminopyrrolidine (yield 60%) and 2,2-dimethylpyrrolidineethane (yield 10%).

A number of derivatives (at the amino group) of the first of the above compounds were prepared with the objective of study of their physiological activity.

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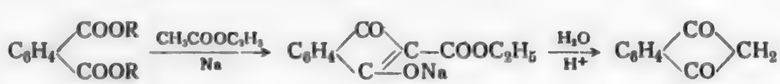
4-NITRO-1,3-INDANEDIONE

G. Ia. Vanag and V. P. Oshkaia

Derivatives of 1,3-indanedione are more and more attracting the attention of chemists. These derivatives include physiologically active substances (blood anticoagulants, rodenticides, antimicrobic substances) as well as valuable analytical reagents (ninhydrin, 2-nitro-1,3-indanedione, etc.). Analogs of indanedione are of particular interest in analysis. It could be expected, for example, that replacement of the benzene ring in ninhydrin or 2-nitro-1,3-indanedione by the naphthalene grouping would give analytical reagents of greater sensitivity or specificity. From this aspect studies have been made of perinaphthindanetrione hydrate [1, 2], 2-nitro-1,3-perinaphthindanetrione [3], and (very recently) benzo- and naphthoindanediones [4]. All of these compounds have properties broadly resembling those of ninhydrin 2-nitro-1,3-indanedione, but they have no special advantages over over the latter.

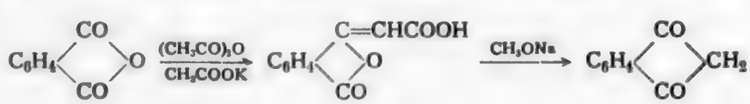
Another route may be followed in the search for new analytical reagents in this group. This is the introduction of various functional groups into the benzene ring of indanedione. Very few derivatives of this class are known as yet, since a procedure for their preparation has not been developed. On the basis of theoretical considerations [5,6] particular interest should be attached to indanedione and its derivatives containing negative (electrophilic) substituents at the benzene ring; we therefore set ourselves the initial task of preparing 4-nitro-1,3-indanedione.

1,3-Indanedione is usually prepared by condensation of diethyl or dimethyl phthalate with ethyl acetate in presence of sodium followed by decomposition of the condensation product (sodium salt of the ethyl ester of indanedionecarboxylic acid) with hydrochloric acid.



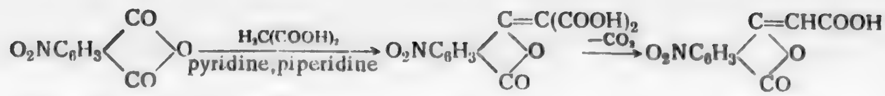
Preparation of a nitroindanedione with the nitro group in the benzene ring would necessitate starting from nitrophthalic acids, but we can at once predict that the nitro group would be lost in the above reaction. This proved to be the case.

A second route to indanedione is condensation of phthalic anhydride with acetic anhydride and isomerization of the resulting phthalylacetic acid to indanedione with the help of sodium methoxide.

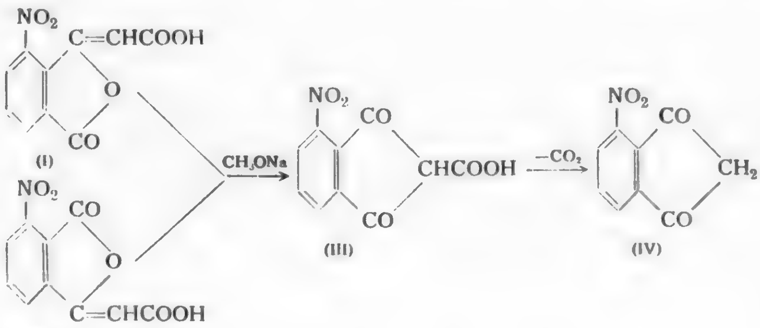


An attempt to prepare nitrophthalylacetic acid from 3-nitrophthalic anhydride was also unsuccessful (only resins were obtained).

On replacing the acetic anhydride in the preceding reaction by malonic acid and performing the condensation in pyridine in presence of a few drops of piperidine, we were able to carry out the reaction at a lower temperature and to obtain nitrophthalylacetic acid.

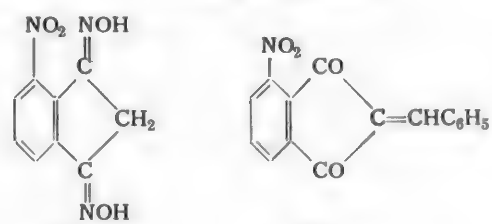


The prepared nitrophthalylacetic acid can theoretically exist in two isomeric forms (I and II). It is not yet certain which of them was obtained; this is not important for their further transformation into nitroindanedione, since rearrangement of either of the acids must give the same 4-nitro-1,3-indanedione (IV), as was confirmed experimentally.



(I) (II) (III) (IV)

The prepared 4-nitro-1,3-indanedione is a yellowish-grey, poorly crystallizing substance. It dissolves in alkalies with an orange-red color; on acidification it is recovered unchanged. It is poorly soluble in water; when heated with water or acetic acid, the solutions rapidly acquire a red-violet color. In all probability this is due to conversion of 4-nitro-1,3-indanedione into anhydro-bis-nitroindanedione or dinitribindone; this conversion evidently goes with greater facility than in the case of indanedione. The presence of two carbonyl groups in 4-nitro-1,3-indanedione was proved by preparation of the dioxime (V). The presence of an active methylene group was proved by formation of a condensation product with benzaldehyde (VI). Consequently, the correctness of formula (IV) for the prepared nitroindanedione is not in doubt.



(V) (VI)

EXPERIMENTAL

Pyridine salt of nitrophthalylacetic acid. 20 g of dry 3-nitrophthalic anhydride was dissolved by heating in 20 ml of freshly distilled pyridine and cooled to 40° (some of the anhydride came down). 10 drops of piperidine and 10 g of dry malonic acid were added. Carbon dioxide came off intensively and the precipitated anhydride gradually went into solution; fresh precipitate started to come down after a short time (its formation was promoted by stirring), and after 3 hours the whole of the mass was solid. The temperature was held at 35-40° during the whole period. After 5 hours the reaction came to an end. The product was 25-32 g (77-98%) of the pyridine salt of nitrophalylacetic acid possibly contaminated with the piperidine salt. This technical product was perfectly suitable for further working-up to 4-nitro-1,3-indanedione. The salt was soluble in water, methanol, ethanol, acetone and dioxane; insoluble in ether and chloroform. Aqueous solutions of the salt have an acid reaction, displace carbon dioxide from sodium bicarbonate and decolorize potassium permanganate solution. After crystallization from acetone, the light-yellow crystals of the salt had m.p. 128°.

Found %: N 8.94. $C_{16}H_{10}O_6N_2$. Calculated %: N 8.91.

Nitrophthalylacetic acid (I or II). 5 g of the pyridine salt of nitrophthalylacetic acid was mixed with 15 ml of sulfuric (1 : 5) or hydrochloric (8.3%) acid, and the solution was filtered. When the solution was allowed to stand, preferably while the sides of the vessel were rubbed with a glass rod, crystals of nitrophthalylacetic acid started to come down. The product was crystallized from 50% alcohol. The yellow crystals had m.p. 184° after recrystallization.

Found %: N 6.07, 5.89. $C_{10}H_5O_6N$. Calculated %: N 5.96

Nitrophthalylacetic acid is poorly soluble in ether and cold water, more easily soluble in hot water; it has good solubility in methanol and ethanol, and is very soluble in acetone and dioxane. The aqueous solutions intensively displace carbon dioxide from sodium bicarbonate and decolorize potassium permanganate solution. The solution in methanol at once gives an orange, gelatinous precipitate with sodium methoxide.

Methyl nitrophthalylacetate. 2 g of nitrophthalylacetic acid, 10 ml of anhydrous methyl alcohol and 6 drops of concentrated sulfuric acid were boiled for 3 hours. The methanol was evaporated off, the crystals of methyl nitrophthalylacetate were separated and crystallized from methanol; the white crystals with m.p. 98° were insoluble in water, soluble in alcohol, and very soluble in acetone. The solution in methanol gives a characteristic yellow-orange coloration with sodium methoxide; on dilution with water a precipitate of the same color comes down.

Found %: N 5.47. $C_{11}H_7O_6N$. Calculated %: N 5.62.

Sodium salt of 4-nitro-1,3-indanedione. 15 g of unrecrystallized, dry pyridine salt of nitrophthalylacetic acid was dissolved with gentle heating in 100 ml of methanol and to the cooled solution was added 2.2 g of sodium in 50 ml of anhydrous methanol in a fine jet with stirring. An orange-yellow solution and a gelatinous precipitate were formed. The mass stood for half an hour with occasional stirring, and the precipitate was collected and washed with methanol. Yield of sodium salt of 4-nitro-1,3-indanedione was 8.5 g (84%). An orange-yellow product was obtained after crystallization from aqueous alcohol; soluble in cold water and very much more soluble in hot water; poorly soluble in alcohol, insoluble in ether and chloroform. The aqueous solution of the salt loses its color on acidification and regains it when made alkaline. The solution turns red-violet when acidified with acetic acid; the color deepens on standing.

Found %: N 6.81, 6.41. $C_9H_4O_4NNa$. Calculated %: N 6.56.

4-Nitro-1,3-indanedione (IV). 5 g of the sodium salt of 4-nitro-1,3-indanedione was triturated in a mortar with 15 ml of dilute (1 : 5) sulfuric acid and remained standing for 30 minutes. The solid at first turned yellow and then gray. It was collected, washed with water and dried in the air, during which operation the 4-nitro-1,3-indanedione acquired a violet-brown shade. Yield 2.9 g (65%), m.p. 133°.

Found %: N 7.35, $C_9H_5O_4N$. Calculated %: N 7.33.

4-Nitro-1,3-indanedione is poorly soluble in cold water; on heating it froms a red-violet solution (dinitrobindone ?). Its solution in dioxane is yellow and the solutions in acetone and alcohols are violet-red. It is sparingly soluble in ether and insoluble in chloroform. It dissolves with an orange-red color in ammonia and in solutions of carbonates.

4-Nitro-1,3-indanedione dioxime (V). 0.2 g of 4-nitro-1,3-indanedione, 0.5 g of hydroxylamine hydrochloride and 0.5 g of sodium acetate in glacial acetic acid were boiled for 5 minutes. The precipitate was collected, washed with water and crystallized from alcohol. Brownish crystals which start to decompose at 210° without melting were formed.

Found %: N 19.22. $C_9H_7O_4N_3$. Calculated %: N 19.18.

2-Benzal-4-nitro-1,3-indanedione (VI). 0.2 g of 4-nitro-1,3-indanedione and 10 drops of benzaldehyde were heated for a short time on a water bath. The mass was boiled with alcohol and the residue of 2-benzal-4-nitro-1,3-indanedione was crystallized from ether. Fine, yellow crystals, m.p. 167° were formed.

Found %: N 5.02. $C_{16}H_9O_4N$. Calculated %: N 5.02.

SUMMARY

Nitrophthalylacetic acid is formed by condensation of 3-nitrophthalic anhydride with malonic acid in pyridine in presence of piperidine. Its rearrangement in presence of sodium methoxide in methanol gives 4-nitro-1,3-indanedione which was characterized by preparation of the dioxime and benzal derivative.

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SYNTHESIS AND POLYCONDENSATION OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE

III. INFLUENCE OF THE STRUCTURE OF THE SUBSTITUTING RADICAL ON THE DIRECTION OF ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

We studied [1] the reductive alkylation of hexamethylenediamine in connection with the use of a series of carbonyl compounds containing radicals of different structures. This work established some relations between the structure of the radical of the carbonyl compound and its reactivity in alkylation. Formaldehyde occupies a special position in the series of carbonyl compounds employed.

It was impossible to perform the reaction with formaldehyde under the same conditions as for other aldehydes. Due to the high basicity of hexamethylenediamine, the added formaldehyde came down in the form of polymer, and hydrogenation was hindered. Alkylation was therefore conducted in a neutral medium, and the hexamethylenediamine was used in the form of the hydrochloride. With a diamine/aldehyde molar ratio of 1 : 2 the main product of reaction (yield about 75%) was unsymmetrical N-dimethylhexamethylenediamine with the formula $(CH_3)_2N-(CH_2)_6-NH_2$. A high-boiling fraction formed at the same time in small quantity contained mainly a trisubstituted diamine. Symmetrical N,N'-dimethylhexamethylenediamine and a monosubstituted derivative could not be detected among the reaction products.

Other methods of methylation of hexamethylenediamine were also tried, using the reactions of Hofmann [2] and Leuckart [3]. The Hofmann reaction with methyl iodide led to unsymmetrical N-dimethylhexamethylenediamine as the main product. The Leuckart reaction (involving reaction of an amine with formaldehyde in presence of formic acid followed by reduction with participation of formic acid) gave a methylation product identical with the products of the Hofmann reaction and of reductive methylation. The higher boiling fractions contained products approximating in composition to tri- and tetramethyl derivatives of hexamethylenediamine.

Consequently, the use of any of the above methods of methylation of hexamethylenediamine causes the second methyl group to enter the diamine molecule preferentially at the already methylated nitrogen (the second free amino group remaining untouched) with formation of unsymmetrical N-dimethylhexamethylenediamine. Even in presence of an excess of hexamethylenediamine a mono derivative is not formed. When the ethyl radical is introduced (in reductive alkylation) the main product (symmetrical N,N'-diethylhexamethylenediamine) is accompanied by a considerable quantity (20-30%) of the unsymmetrical N-disubstituted derivative. Introduction of n-propyl is accompanied by formation of a little unsymmetrical N-disubstituted derivative. Introduction of isopropyl and other higher radicals (n-butyl, isobutyl, unsymmetrical butyl) leads to symmetrical N,N'-disubstituted hexamethylenediamine as the predominant product (87-95% yield). An unsymmetrical disubstituted product could not be detected. The observed relations are summarized in Table 1.

The tendency of a second substituting methyl radical to attach itself preferentially at an already substituted group and not at the free amino group of the diamine is presumably due to the increased susceptibility to coordination of the unshared electron pair at the nitrogen as the result of shift of the electron density under the influence of the positive inductive effect of the substituent. The direction of the reaction depends, however, in great measure also on the size and spatial structure of the groups.

TABLE 1

Influence of the Structure of the Alkylating Compound on the Direction of N,N'-dialkylation of Hexamethylenediamine

Alkylating compound	Yield on basis of reacted hexamethylenediamine (in %)	
	symmetrical N,N'-dialkyl derivative	unsymmetrical N-dialkyl derivative
Formaldehyde	Not detected	72
Acetaldehyde	40	20
Propionaldehyde	58	2
Acetone	93	Not detected
Butyraldehyde	85	The same
Methyl ethyl ketone	90	" "

The steric hindrance created by the methyl group is insignificant, and the directivity of disubstitution at the one NH_2 group is governed by the enhancement of activity of the amino group under the influence of the positive inductive effect of the substituent. When an ethyl group is introduced the enhancement of reactivity of the amino group under the influence of a substituent is already lowered to a certain degree by the increasing steric effect caused by the ethyl being larger than the methyl. Starting from isopropyl, the shielding effect acquires a dominating influence and governs the preferential directivity towards N,N'-disubstitution.

Preliminary experiments on the introduction of tert.butyl and trimethylsilyl into the amino group of hexamethylenediamine (using the Hofmann reaction) were undertaken with the aim of preparing N-alkylated hexamethylenediamines with highly branched substitutuents. The experiments showed that tert.butyl cannot be introduced under the experimental conditions. Trimethylsilyl easily replaces the 2 hydrogen atoms in each of the amino groups to give preferentially a tetrasubstituted diamine. This difference in alkylation behavior is evidiently due to the strong shielding of the central carbon atom in tert.butyl, whereas the steric influence does not prevent interaction of trimethylsilyl with the nitrogen of the amino group because the atomic radius of silicon (1.17 A) is much larger than that of carbon (0.77 A).

EXPERIMENTAL

Reductive methylation of hexamethylenediamine – Into a autoclave (for reduction procedure see [1]) were charged a solution of 17.45 g of hexamethylenediamine in 30 ml of alcohol neutralized with 37.5 ml of concentrated hydrochloric acid, 9.0 g of formaldehyde (in the form of 29 ml of 37% formalin) and 0.2 g of platinum oxide. The diamine/aldehyde molar ratio was 1 : 2. Absorption of hydrogen at room temperature was observed for 40 minutes. The pressure dropped from 102 to 19 atm , corresponding to 320 millimoles of hydrogen (100% of the theoretical quantity). After the catalyst had settled, the mixture was decanted and the diamine displaced from the salt with 150 ml of 70% NaOH; it was dried over potassium carbonate and vacuum-fractionated in a nitrogen atmosphere. The vapor temperature quickly rose to 67-68° (2 mm) and the greater portion of the product came over in this range. The vapor temperature then rose steadily from 69 to 120° (2 mm) (a second fraction was collected). The quantity of still residue was insignificant. The main fraction – 67-68° (2 mm) – weighed 16.1 g (yield 75% on the diamine taken into reaction) and consisted of unsymmetrical N-dimethylhexamethylenediamine, as evident from the analytical results.

B.p. 67-68° 2 mm, d_4^{25} 0.831, n_D^{25} 1.447, MR_D 45.9; calculated 46.3.

Found %: N (total) 19.4; NH_2 9.6*, M (Rast method) 150. $C_8H_{20}N_2$. Calculated %: N 19.4; NH_2 9.7; M 14 4.

Judging by the content of total nitrogen (16.8%) the 69-120° (2 mm) fraction is a mixture of tri- and tetramethyl substituted derivatives with nitrogen contents of 17.7 and 16.3%.

Reductive ethylation of hexamethylenediamine. A solution of 11.6 g of hexamethylenediamine in 67 ml of alcohol, 8.8 g of acetaldehyde (diamine/aldehyde molar ratio 1: 2) and 0.2 g of platinum oxide were charged into a metal ampoule cooled to -8 to -10°. The aldehyde was added in a hydrogen atmosphere. Absorption of hydrogen was observed for 30 minutes. The pressure dropped from 110 to 61 atm., corresponding to 254 milli-

* The percentage of NH_2 was determined by the Van Slyke method and expressed as percentage of N.

moles of hydrogen (100% of the theoretical quantity). After the settling of the catalyst, the solvent was distilled off; the residue was dissolved in ether, dried over potassium carbonate, and (after removal of the ether) fractionated in vacuo in a nitrogen medium. The first fraction came over at 67-98° (5 mm) and contained a considerable quantity of hexamethylenediamine (total nitrogen content 21.3%). A second fraction was collected at 98-105° (5-7 mm) and its nitrogen content (16.2%) corresponded to the diethyl derivative of hexamethylenediamine. The higher boiling products coming over at 106-205° (5 mm) contained more highly alkylated derivatives (nitrogen content 13.7%).

The 98-105° (5-7 mm) fraction was analyzed for its content of NH_2 groups (found 1.9% calculated as nitrogen). The result corresponded to a mixture of 76% of symmetrical N,N'-diethylhexamethylenediamine and 24% of unsymmetrical N-diethylhexamethylenediamine. A second fractionation gave a narrower cut at 101-105° (5-7 mm) which contained 96% of the symmetrical derivative. Analytical data and yields are listed in [1]. The latter publication also describes the synthesis of N,N'-diisopropyl and N,N'-di-n-butyl derivatives of hexamethylenediamine.

Alkylation of hexamethylenediamine with tert.butyl chloride or bromide. Experiments were at first performed in a flask with a reflux condenser and stirrer. 11.6 g of diamine was reacted with 18.5 g of tert. butyl chloride; the reaction was carried out both with and without a solvent (dioxane and pyridine, each in quantity of 30 ml). The duration of the reaction was 2-2.5 hours at a bath temperature of 100-125°. A weighed sample was dissolved in methanol and neutralized with HCl (1 : 1); the methanol was evaporated off and the residue dissolved in water. The solution was analyzed for its content of NH_2 groups by the Van Slyke method. The amount of unreacted diamine was 97.8-98.4% of the original quantity.

Experiments on alkylation in sealed glass ampoules were also run in which 4.62 g of tert. butyl chloride or 6.85 g of tert. butyl bromide was added to 2.90 g of hexamethylenediamine. The ampoules were kept at 100° for 48 hours. With progressive heating the separation of a crystalline material was observed. When the ampoules were opened, 70 and 96 ml of gas respectively were evolved (evidently isobutylene). Analysis of the mixtures for the NH_2 group showed that the quantities of unsubstituted diamine were respectively 99.0 and 99.2% of the original quantities.

Introduction of trimethylsilyl. Experiments were run at first in a flask with a reflux condenser and stirrer. 28.4 g of trimethylchlorosilane was added gradually to a solution of 14.5 g of hexamethylenediamine in 30 ml of anhydrous pyridine (the apparatus was shielded against access of moisture from the air by means of calcium chloride tubes). Reaction was effected at 125° for 4 hours. The reaction mixture, in which a gelatinous precipitate appeared, was repeatedly extracted with ether. After the ether and pyridine had been distilled off, the residue was fractionally distilled in vacuo in a nitrogen atmosphere. Nearly the whole of the product came over at 150-165° (2 mm). Analytical results are presented in Table 2.

TABLE 2

Analyses of Fractions of Silico Derivatives of Hexamethylenediamine

Boiling point (pressure in mm)	Weight (in g)	Content (in %) of		Theoretical N content (in %)	
		N (by titration	NH_2 group (Van Slyke techn.)	trisubstituted	tetrasubstituted
150—165° (2)	4.8	7.4	7.2	8.4	7.0
153—170 (2)	2.3	7.8	7.8		

The tabulated data show that the prepared compounds approximate in composition to tri- and tetra substituted derivatives, and the N – Si bond is broken under the conditions of the Van Slyke determination.

SUMMARY

1. It is shown that the preferred course of the reductive alkylation of hexamethylenediamine which is in the direction of symmetrical N,N'-dialkylation is governed by two opposing influences; the enhanced reactivity of the substituted amino group and the steric effect of the substituent.

2. It was established that the reaction goes exclusively in the direction of symmetrical N,N'-disubstituted derivatives when the alkylating radical is isopropyl or higher.

3. Difficulties are encountered in obtaining the pure symmetrical derivative of hexamethylenediamine when introducing the ethyl and n-propyl radicals. When the methyl radical is introduced the reaction is wholly directed towards formation of the unsymmetrical substitution product.

4. It is shown that the tert.butyl group could not be introduced into the amino group of hexamethylenediamine under the conditions of reaction, whereas trimethylsilyl easily substitutes both of the hydrogen atoms with formation of a tetrasubstituted derivative. This difference in behavior is explained by the difference in the steric effects of the two types of groups due to the difference in atomic radii of silicon and carbon.

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*See C.B. Translation.

SYNTHESIS OF N-ALKYL DERIVATIVES OF HEXAMETHYLENEDIAMINE AND THEIR POLYCONDENSATION

V. SOME PROBLEMS OF THE KINETICS OF THE REDUCTIVE ALKYLATION OF HEXAMETHYLENEDIAMINE

A. L. Klebanskii and M. S. Vilesova

A. Dependence of the reaction velocity on the reaction conditions. Results obtained in a study of the synthesis of N-substituted diamines, as well as special experiments, permitted calculations with the objective of determination of the reaction order and allowed the comparison of the relative reaction rates with different alkylating compounds.

A study of the reductive alkylation of hexamethylenediamine with aldehydes and ketones both at high (100-50 atm pressure and at atmospheric pressure showed that the reaction is of zero order. This order is evidently determined by sorption which is limited by the step of diffusion of the reactants from the solution to the catalyst. It was shown that the reaction rate does not depend on the concentration of the components and on their change during the reaction. Results are plotted in Figs. 1-5.

Study of reductive alkylation under pressure of 40-10 atm revealed a nonlinear dependence of the reaction rate on time, as we see from Figs. 6 and 7. Calculation showed that the reaction under these conditions is approximately first order in dependence on the pressure and consequently also on the hydrogen concentration in the liquid phase. The velocity constants of this reaction, in dependence on the quantity of absorbed hydrogen, are calculated from the equation for a first-order reaction (Table 1).

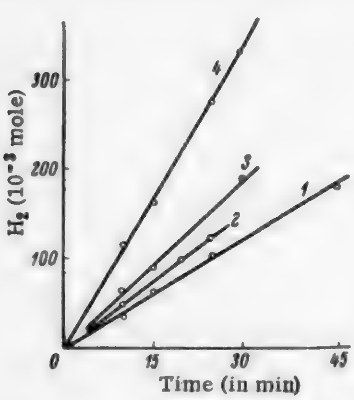

Fig. 1. Reduction of a mixture of hexamethylenediamine and carbonyl compound in the 100-50 atm pressure range. 1) propionaldehyde, 2) acetone, 3) methylethyl ketone, 4) butyraldehyde.

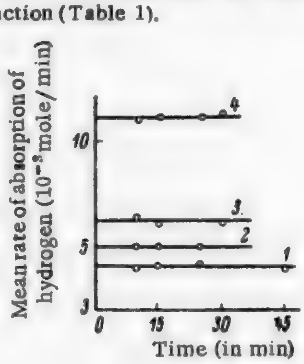

Fig. 2. Mean rate of absorption of hydrogen (according to Fig. 1) at 100-50 atm 1) propiondehyde, 2) acetone, 3) methyethyl ketone, 4) butyraldehyde

The observed difference in the course of reductive alkylation in different pressure regions in respect of reaction order may be explained in the following manner. During reduction at atmospheric pressure the pressure remains constant throughout the whole of the reaction period and has no influence on the reaction velocity

TABLE 1

Velocity Constants of the Reductive Alkylation of Hexamethylenediamine (in respect of hydrogen). P = 4-10 atm., Temperature 25°

Reaction time (min)	Alkylating compound							
	acetone		methyl ethyl ketone		propionaldehyde		n-butyraldehyde	
	$K \cdot 10^2$	percentage transf.	$K \cdot 10^2$	percentage transf.	$K \cdot 10^2$	percentage transf.	$K \cdot 10^2$	percentage transf.
2.5	3.20	28	2.36	21	1.84	17	1.32	12
5.0	3.44	54	2.50	42	1.92	33	1.40	24
7.5	3.22	70	2.45	56	1.88	46	1.39	36
10.0	—	—	2.23	66	1.76	55	1.26	42

During reduction in the 100-50 atm. pressure range there is evidently complete sorptive saturation of the catalyst with hydrogen even at the lower pressure limit, and change of pressure exerts no influence on the rate of reductive alkylation. Reduction of the hexamethylenediamine–carbonyl compound mixture at 40-10 atm is associated with absence of complete saturation of the catalyst with hydrogen, and the degree of saturation evidently depends on the magnitude of the pressure. The first-order reaction is determined in this case by the falling hydrogen pressure during the reaction.

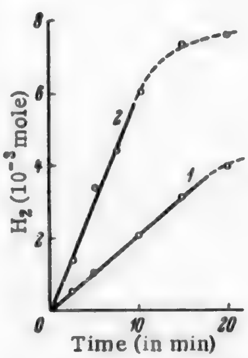

Fig. 3. Reduction of a mixture of hexamethylenediamine and carbonyl compound at atmospheric pressure (degree of conversion approx. 75% . 1) acetone, 2) butyraldehyde

B. Influence of the structure of the alkylating compound on the velocity of reductive alkylation of hexamethylenediamine. The reaction rate is markedly dependent on the structure of the alkylating aldehyde or ketone. Data for reduction under pressure are plotted in Fig. 8. The rate of this reaction is determined by the rate of chemisorption of the starting components on the catalyst. In the cases in question, where the diamine is always the same substance, the factor governing the character of the reaction is the structure of the alkylating carbonyl compound.

An insight into the influence of structure of the carbonyl compound on the reaction rate during reductive

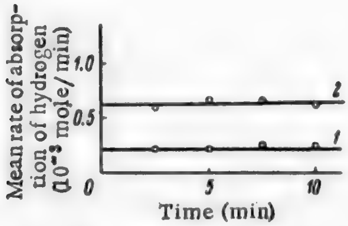

Fig. 4. Mean rate of absorption of hydrogen (according to Fig. 3) at pressure of 760 mm. 1) acetone, 2) butyraldehyde

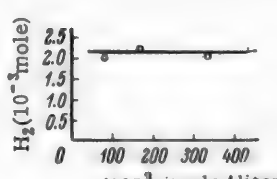

Fig. 5. Dependence of quantity of absorbed hydrogen (in reduction of a mixture of hexamethylene diamine and butyraldehyde) on the initial concentration of reactants (after 20 minutes).

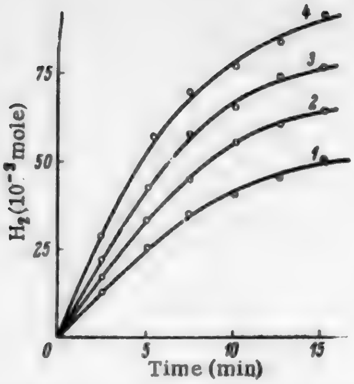

Fig. 6. Reduction of a mixture of hexamethylenediamine and carbonyl compound in the pressure range of 40-10 atm. 1) butyraldehyde, 2) propionaldehyde 3) methyethyl ketone, 4) acetone.

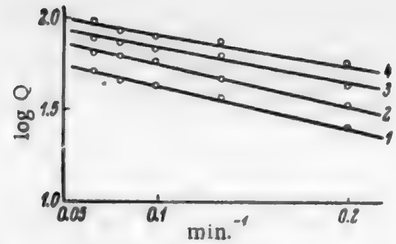

Fig. 7. Dependence of the logarithm of the quantity of absorbed hydrogen (Q in mole · 10^{-3}) on the reciprocal of the time. 1) butyraldehyde, 2) propionaldehyde, 3) methylethyl ketone, 4) acetone.

alkylation is obtained from Table 2 which lists the velocity constants with different alkylating agents (calculated with respect to hydrogen at 25°).

The influence of the structure of the carbonyl compound on the course of reductive alkylation (determined by the rate of chemisorption) is evidently associated with the change of the polarization of the C = O bond in dependence on the character of the aliphatic radicals linked with the carbonyl. In presence of methyl groups the electron density is inductively shifted to the oxygen and this increases its electronegative character and in turn the polarizability of the C^+-O^- bond. The number of methyl groups and their distance from the carbonyl determine the degree of this polarization.

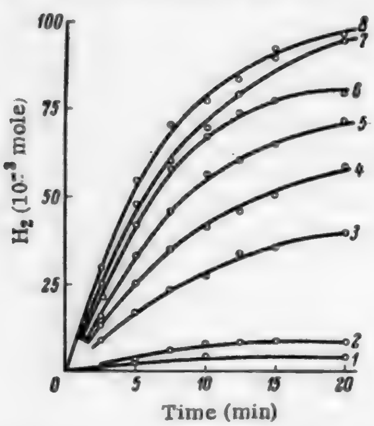

Fig. 8. Dependence of the rate of reductive alkylation on the structure of the alkylating compound. 1) diisopropyl ketone, 2) diisobutyl ketone, 3) isobutyraldehyde , 4) n-butyraldehyde, 5) propionaldehyde, 6) methylethyl ketone, 7) acetaldehyde . 8) acetone.

The polarity of a molecule and in turn its activity in chemisorption processes can be quantitatively characterized by the magnitude of the dielectric constant. The value of ϵ for some aldehydes and ketones are presented in Table 3.

On comparing the data of Tables 2 and 3 we see that carbonyl compounds are arranged in the same order in respect of magnitudes of velocity constants and magnitudes of dielectric constants. Although values of ϵ could not be found in the literature for isobutyraldehyde, we can assume that the branched structure and the presence of two methyl groups must cause the polarization of the C = O bond to be greater than in n-butyraldehyde. Experiments show, however, that alkylation with isobutyraldehyde proceeds more slowly than with n-butyraldehyde. This effect may be attributed to the steric hindrance arising from the branched structure of the iso compound.

The steric factor plays an important part in all of the cases of alkylation in question and depresses the influence of the polarizing factor, as demonstrated in particular in the alkylation with highly branched ketones (which have a considerable inductive effect). It does not appear possible in the present work to quantitatively characterize these opposing effects (increase of polarization and intensification of the steric effect) by the process of chemisorption. It only remains to note that when highly branched radicals are introduced (by alkylation with the help of diisopropyl and diisobutyl ketones) the screening effect definitely predominates, and this is reflected in the exceptional slowness of the reaction even at higher temperature, notwithstanding that the polar effect must here be considerable.

TABLE 2

Velocity Constants of the Reductive Alkylation of Hexamethylenediamine with Various Aldehydes and Ketones

Alkylating compound	$K_{mean} \cdot 10^2$ (with respect of hydrogen
Acetone	3.29
Acetaldehyde	2.81
Methyl ethyl ketone .	2.38
Propionaldehyde . . .	1.85
n-Butyralde	1.34
Isobutyraldehyde	0.86
Diisobutyl ketone . .	0.24

TABLE 3

Dielectric Constants of Aldehydes and Ketones [1, 2]

Carbonyl compound	ε	Temperature
Acetone	21.4	20°
Acetaldehyde	22.2 *	10
Methyl ethyl ketone .	18.0	20
n-Butyraldehyde	13.8	26

* The value of ε falls with rising temperature, and for acetaldehyde at 20° it will evidently be lower than for acetone

Consequently, the velocity of reductive alkylation of hexamethylenediamine in depending on the structure of the carbonyl compound is determined by two opposing influences: the polarizing effect of the substituting radical on the C = O group on the one hand, and the steric factor on the other hand. Polarization plays the predominant part in the case of lower aldehydes and ketones whose steric effect is insignificant, while the screening effect is more powerful in the case of higher members of the series with highly branched structures.

EXPERIMENTAL

Reductive alkylation of hexamethylenediamine at atmospheric pressure. Experiments were performed in a Willstatter hydrogenation vessel of 100 ml capacity which was attached to a shaking machine and immersed in a thermostat whose temperature was kept constant to within 0.3° with the help of a contact thermometer and an electronic relay. A weighed amount of catalyst in alcohol was placed in the vessel (in the thermostat) connected to a gas buret filled with hydrogen (supplied from a gasholder) and purged with 4 volumes of hydrogen. The shaking machine was then started, the hydrogenation vessel was linked with the buret and the platinum oxide was reduced to platinum black. The latter was saturated with hydrogen until no more gas was absorbed. A small beaker containing a weighed quantity of the carbonyl compound was suspended from a movable piston pushed through the stopper. The weighed sample of hexamethylenediamine in alcohol was placed directly in the hydrogenation vessel which was again purged with 4 volumes of hydrogen. The piston was then pushed down in a hydrogen atmosphere and the beaker with the carbonyl compound fell into the hexamethylenediamine solution. At that instant the shaking machine was set in motion and measurement was made of the quantity of hydrogen (in ml) absorbed in unit time (the time was measured with a stopwatch). The progress of the reaction was followed from the volume of H_2 absorbed. A preliminary determination had been made of the number of shakings required for the process to proceed in the kinetic region (320 per minute).

Experiment 1. To a solution of 0.464 g of hexamethylenediamine in 23.4 ml of alcohol were added 0.576 g of butyraldehyde and 0.2 g of platinum oxide. The reaction was conducted at 20°. Data for hydrogen absorption are plotted in Fig. 3.

Experiment 2. To a solution of 0.232 g of hexamethylenediamine in 24.4 ml of alcohol were added 0.232 g of acetone and 0.05 g of platinum oxide. Reaction was conducted at 16°. Data for hydrogen absorption are plotted in Fig. 3.

Experiment 3. To solutions of 0.232 g of hexamethylenediamine in 24.4 ml of alcohol, 0.464 g in 24.0 ml of alcohol and 0.961 g in 22.6 ml of alcohol were added, respectively, 0.288, 0.576 and 1.193 g of butyraldehyde and 0.050 g of platinum oxide. The total volume in each case was kept at 25.0 ml, while the concentrations of diamine in moles/liter $\times 10^3$ were 80, 160 and 134. Reaction was performed at 25°. Data for the hydrogen absorption are plotted in Fig. 5.

Study of the dependence of the rate of reductive alkylation on the structure of the alkylating agent. Experiments were performed under pressure in the autoclave described earlier [3]. Constant conditions that would facilitate comparison of individual experiments were established by the provision of the autoclave with a metal jacket through which water was circulated from an ultrathermostat. Constancy of temperature inside the autoclave ($30 \pm 0.2°$) was checked by a thermocouple in a pocket (sensitivity 0.2°). A 60-atm. pressure gage graduated in atmospheres enabled the pressure drop to be recorded to an accuracy of 0.25 atm. The volume of the reaction mixture and the initial pressure were kept strictly constant in all of the experiments. In each case the number of shakings was 280 per minute. Into the autoclave were charged the solution of the weighed sample of hexamethylenediamine in alcohol, the catalyst and the alkylating agent (the latter in a thin-walled sealed glass ampoule containing an internal sharp-tipped projection). As already indicated, the autoclave was purged with hydrogen, the necessary pressure was established, and the autoclave was placed on the shaking machine and thermostated for 20 minutes. The shaking machinism was then put in motion, the glass ampoule broke immediately (as reflected in commencement of pressure drop), and the components were mixed in a hydrogen atmosphere. The pressure drop was recorded by the gage and the duration was noted by stopwatch.

The amounts of carbonyl compound taken for 5.80 g of hexamethylenediamine were 4.40 g of acetaldehyde, 5.80 g of propionaldehyde or acetone, 7.20 g of n-butyraldehyde, isobutyraldehyde or methylethyl ketone, 11.40 g of diisopropyl ketone, and 14.20 g of diisobutyl ketone. The volume of the mixture was made up to 45 ml (roughly) by addition of alcohol. In each case the quantity of platinum oxide was 0.05 g, and the initial pressure was 40 atm. Data for hydrogen absorption are plotted in Figs. 6 and 8. The velocity constants of the respective reactions were calculated from these data.

Determination of the reaction order in reductive alkylation of hexamethylenediamine at above 50 atm. Experiments were performed in the autoclave under the previously described conditions.*

Experiment 1. 17.40 g of hexamethylenediamine in 51 ml of alcohol was treated with 17.40 g of propionaldehyde and 0.05 g of platinum oxide. Initial pressure 126 atm.

Experiment 2. 11.6 g of hexamethylenediamine in 19.0 ml of alcohol was treated with 11.6 g of acetone and 0.05 g of platinum oxide. Initial pressure 98 atm.

Experiment 3. 29.0 g of hexamethylenediamine in 17.0 ml of alcohol was reacted with 36.0 g of n-butyraldehyde in presence of 0.20 g of platinum oxide. Initial pressure 130 atm.

Experiment 4. 17.0 g of hexamethylenediamine in 46.0 ml of alcohol was reacted with 36.0 g of methylethyl ketone in presence of 0.10 g of platinum oxide. Initial pressure 96 atm.

The course of hydrogen absorption is plotted in Fig. 1.

SUMMARY

1. It was established that the reductive alkylation of hexamethylenediamine at normal pressure and at pressures about 50 atm. is a reaction of zero order; in the 10-40 atm. pressure range it is a first-order reaction. The difference in behavior is due to incomplete sorptive saturation of the catalyst in the 10-40-atm. range.

2. It was shown that the rate of reductive alkylation of hexamethylenediamine is determined by the relative polarity of the alkylating compounds on the one hand and by the steric influence of their structure on the other hand. The second factor plays a predominant part only in the case of higher carbonyl compounds with considerable branching.

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*The 60-atm. pressure gauge was replaced by a 250-atm. gauge.

**See C.B. Translation.

THE FERMENTATIVE SYNTHESIS OF N-PEPTIDES FROM O-PEPTIDES OF β-HYDROXYAMINO ACIDS

M. M. Botvinik and S. M. Avaeva

In a study of the specific properties of N-peptides of serine and threonine, we showed [1] that they are susceptible not only to intramolecular but also to intermolecular rearrangement. The reaction goes according to the equation

$$\begin{array}{l} CH_2CHCOOH \\ |\quad\ \ | \\ O\quad NHCOC_6H_5 \\ | \\ COCH(R)NHCOC_6H_5 \end{array} + R'NH_2 \rightarrow C_6H_5CONHCH(R)CONHR' + \begin{array}{l} CH_2OH{-}CH{-}COOH \\ \qquad\qquad\ \ | \\ \qquad\qquad NHCOC_6H_5 \end{array}$$

$$R'{=}H,\ CH(R'')CO_2C_2H_5.$$

When O-peptides of N-benzoylserine and threonine are reacted with ammonia, the reaction is nearly instantaneous, but with esters of amino acids and peptides, the process is slow at elevated temperatures and the yield is poor. If, however, the reaction is performed in presence of chymotrypsin, it goes with great facility and leads to derivatives of peptides of the L-series [2]. It seemed to us that this reaction, in which O-peptides of β-hydroxamino acids are carriers of amino acid residues in the fermentative synthesis of peptides. is of interest in connection with possible secondary reactions in nature. In the present work we investigated a number of other substances from this aspect. Experiments were run with N-benzoyl-O-benzoylphenyl-alanyl-serine, N-benzoyl-O-benzoylglycyl-serine and N-benzoyl-O-benzoylphenylalanyl-threonine. Acceptors for the acylamino acid residues were the ethyl esters of glycine, phenylalanine, glycylglycine and leucylglycine. All of the starting compounds were racemic, and in all cases the optically active peptides were obtained. Results of the investigations are set forth in the table. Experiments were performed at room temperature and at a pH of 7.8-8. The reaction went with particular ease when using N-benzoyl-O-benzoylphenylalanylserine which reacted with esters of glycine, phenylalanine, glycylglycine and leucylglycine in the course of 10-30 minutes. Precipitation of the esters of the benzoylpeptides was completed within this period (see experiments 1-4). The yield of the latter was 46-68%. The experiment with N-benzoyl-O-benzoylphenylalanylthreonine went in similar fashion, although the yield of peptide ester was only 26% (experiment 6). No precipitate was formed in reactions of N-benzoyl-O-hippurylserine with the ethyl ester of glycine; the reaction was therefore run for 48 hours, and inspissation of the solution led to separation of 15% of the ester of benzoylglycylglycine (experiment 5). Change of reaction conditions had little influence on the synthesis of peptides. Rise of temperature to 34° shortened the process, but change of pH to 8.5 had no appreciable effect.

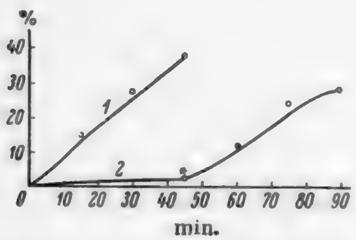
Preliminary experiments were run with N-benzoyl-O-hippurylserine and N-benzoyl-O-benzoylvalylserine, using esters of phenylalanine, glycylglycine and leucylglycine as acceptors of amino acid residues. These experiments gave unsatisfactory results. The reason was evidently not the hydrolysis of the O-peptide by chymotrypsin since the same N-benzoyl-O-peptides of serine that had not reacted with amino acid esters were not split by the ferment. Experiments on hydrolysis of N-benzoyl-O-peptides of serine showed that N-benzoyl-O-benzoylphenylalanylserine is hydrolyzed to the extent of 10% in 10 minutes by chymotrypsin under selected conditions, while N-benzoyl-O-benzoylvalylserine and N-benzoyl-O-benzoylglycylserine are not altered in 90 minutes (see diagram. These facts may be evidence in support of the theory [3] that both of the processes –

synthesis and hydrolysis of peptides – proceed via the same intermediate compound, which is formed by the amino acid residue and the ferment.

Summary of Fermentative Syntheses

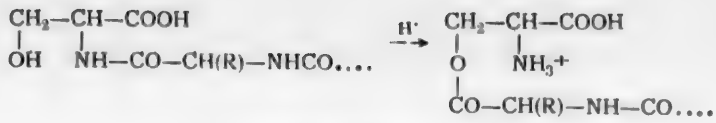
Expt. No.	First component		Second component		Yield of peptide ester (in %)	Reaction conditions		
	R	R′	R″	R‴		time (min)	temp.	pH
1	H	$C_6H_5CH_2$	H	OC_2H_5	48	10	20°	8.1
2	H	$C_6H_5CH_2$	$C_6H_5CH_2$	OC_2H_5	46	10	20	7.8
3	H	$C_6H_5CH_2$	H	$NHCH_2CO_2C_2H_5$	+	30	20	7.8
4	H	$C_6H_5CH_2$	iso -C_4H_9	$NHCH_2CO_2C_2H_5$	68	10	20	7.8
5	H	H	H	OC_2H_5	15	48 hours	20	8
6[2]	CH_3	$C_6H_5CH_2$	H	OC_2H_5	26	10	20	7.8

The ability of esters of amino acids to form peptides under the influence of chymotrypsin was discovered by Brenner and co-workers [4]. They showed that, in presence of chymotrypsin, esters of methionine and threonine form a mixture of peptides, their esters and amino acids. The reaction proceeded for 20-40 hours at 22-38° and a pH of 9. Tauber [5] found that at pH 8.8 and 37° the ethyl ester of phenylalanine, to whose solution chymotrypsin had been added, forms a peptide ester. The latter begins to come down after 10 minutes. Its yield was 10%. I. L. Kaganova and V. N Orekhovich [6] studied this reaction in the case of the ethyl ester of threonine at pH 9, a temperature of 37° and an experimental period of 10 minutes to 2 hours. They found that the reaction is selective: the ethyl ester of tyrosine reacted with glutamine, asparagine, leucylglycine, g glycylglycine, etc., but not with aspartic acid, glutamic acid, glycyltryptophan, glycine and leucine. Lestrovaia and Mardashev [7] found that the ethyl ester and the amide of phenylalanine behave even more selectively. A large number of diverse amino acids and peptides were investigated, and phenylalanine was found to react only with itself.



Hydrolysis of N-benzoyl-O-benzoylphenylalanylserine by chymotrypsin. 1) experiment with ferment, 2) experiment without ferment (• denotes point of addition of ferment).

The investigations that we undertook are different from those described in the literature. Experiments were performed with esters of amino acids in which the alcoholic residue was a β-hydroxyamino acid, i.e., the compounds under investigation more closely resembled natural substances. The esters used were not those of amino acids themselves but of their benzoyl derivatives, so that the reaction stopped at the dipeptide stage. The reaction required a shorter period of time at a lower pH and with a smaller quantity of ferment. In our opinion the reactions in question are not devoid of interest if only because O-peptides of β-hydroxyamino acids are formed with relative ease from N-peptides of β-hydroxyamino acids in an acid medium according to the equation [8]:



EXPERIMENTAL

1. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoyl-D,L-serine with the ethyl ester of glycine. a) In presence of chymotrypsin. 500 mg of O-benzoylphenylalanyl-N-benzoylserine was dissolved in hot alcohol, neutralized with 1 N sodium hydroxide and mixed in presence of 2 ml of phosphate buffer (pH 7.9) with a solution of 700 mg of the hydrochloride of the ethyl ester of glycine in the equivalent quantity of 1 N caustic alkali. To the reaction mixture was added 3-5 mg of chymotrypsin. The experiment was performed at a pH of 8.1. After a few minutes, long needles started to come down. After 8-10 minutes the precipitate was filtered and recrystallized from aqueous alcohol. The ethyl ester of benzoyl-L-phenylalanylglycine had m.p. 148-149°. Its yield was 24% calculated on the racemate and 48% on the L-antipode of the ester of phenylalanine [2].

Found %: C 67.76; H 6.42; N 7.92. $C_{20}H_{22}O_4N_2$. Calculated %: C 67.70; H 6.21; N 7.92.

After the mother liquor had stood for a long period or after a fresh portion of chymotrypsin had been added to it, no separation of the ethyl ester of benzoylphenylalanylglycine was observed.

b) Blank experiment without ferment. 400 mg of O-benzoylphenylalanyl-N-benzoyl serine was dissolved in hot alcohol, neutralized with 1 N solution of caustic alkali and mixed in presence of 2 ml of phosphate buffer (pH 7.9) with a solution of 500 mg of the hydrochloride of the ethyl ester of glycine in the equivalent quantity of alkali. The pH of the solution was brought to 8.1. The slightly cloudy solution did not change in the course of several hours. After 18 hours the salt of 0-benzoylphenylalanyl-N-benzoylserine and the ethyl ester of glycine was isolated. M.p. 147-148°. The salt is easily soluble in water and gives a positive ninhydrin reaction. The result of the Van Slyke nitrogen determination is given below.

Found %: NH_2 2.52. Calculated %: NH_2 2.48.

c) In presence of diisopropyl fluorophosphate. 300 mg of O-benzoylphenylalanyl-N-benzoylserine was brought into reaction with 420 mg of the ethyl ester of glycine hydrochloride as described above. To the reaction mixture was added 3-5 mg of chymotrypsin which ahd previously been mixed (for 2 hours) with 2 ml of phosphate buffer and a drop of diisopropyl fluorophosphate. The solution remained transparent for 18 hours. Addition of a fresh portion of ferment led to slow precipitation (in the course of 3 hours) of a small quantity of the ethyl ester of L-benzoylphenylalanylglycine. Yield 15 mg. M.p. 146-147°.

2. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoylserine with the ethyl ester of D,L-phenylalanine. 1 g of the ethyl ester of phenylalanine hydrochloride was dissolved in the equivalent quantity of 1 N alkali. The resulting oil was decanted and mixed with a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali. Addition was then made of the mother liquor remaining after separation of the ester of phenylalanine. This was followed by a phosphate buffer and (at pH 7.8) . chymotrypsin (2-3 mg). Particles of the ferment began to intermingle nearly instantaneously with the precipitate which consisted of the ethyl ester of benzoyl-L-phenylalanylphenylalanine. After an hour the reaction mixture was diluted with water and the precipitate was filtered off. The yield of ethyl ester of benzoyl-L-phenylalanylphenylalanine was 90 mg (46% calculated on the O-benzoyl-L-phenylalanyl-N-benzoylserine). M.p. (after numerous recrystallizations from aqueous alcohol) 146-148°, $[\alpha]_D^{18}$ $-36.5 \pm 1.2°$ (0.1204 g in 315 ml of alcohol).

Found %: C 73.09, 73.16; H 6.36, 6.56. $C_{27}H_{28}O_4N_2$. Calculated %: C 72.98; H 6.31.

The mother liquor remaining after separation of the ester of the benzoyl dipeptide was acidified. The precipitate was found to be optically active with $[\alpha]_D^{18}$ $+11.3 \pm 0.9°$ (0.2703 g in 35 ml of anhydrous alcohol). A blank experiment without ferment was run under similar conditions. No outward change was observed after an hour. Addition of chymotrypsin to the solution caused immediate precipitation of a substance identical with that isolated from the main experiment with the ethyl ester of benzoyl-L-phenylalanylphenylalanine.

In another blank experiment, ferment was not added to the reaction mixture but the solution was acidified In this case, out of 100 mg of O-benzoylphenylalanyl-N-benzoyl serine taken for the experiment, 73 mg was recovered.

3. Reaction of O-benzoyl D,L-phenylalanyl-N-benzoylserine with the ethyl ester of D,L-leucylglycine. To a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali was added a solution of 1.26 g of the hydrochloride of the ethyl ester of leucylglycine in the equivalent quantity of 1 N alkali, 2 ml of phosphate buffer and (at a pH of 7.8) 2-3 mg of chymotrypsin. A precipitate at once started to come down. It was filtered off on the following day and recrystallized from aqueous alcohol. Yield of ethyl ester of benzoyl-L-phenylalanylleucylglycine 150 mg (68%); m.p. 198.5-199°; $[\alpha]^{20}_D$ −46.3 ± 3.0° (32.8 mg in 2 ml of alcohol).

Found %: C 66.68, 66.57; H 7.31, 7.37; N 9.07, 9.25. $C_{26}H_{33}O_5N_3$. Calculated %: C 66.81; H 7.06; N 8.99.

In a similar blank experiment, a minute quantity of the ethyl ester of benzoylphenylalanine with m.p. 94-95° came down after 3 days.

4. Reaction of O-benzoyl-D,L-phenylalanyl-N-benzoylserine with the ethyl ester of glycylglycine. To a solution of 460 mg of O-benzoylphenylalanyl-N-benzoylserine in the minimum quantity of alcohol and the equivalent quantity of 1 N alkali was added a solution of 1.0 g of the hydrochloride of the ethyl ester of glycylglycine in the equivalent quantity of alkali, 2 ml of phosphate buffer and (at pH 7.82) 2-3 mg of chymotrypsin. An emulsion immediately started to form around the particles of ferment and slowly settled down in the form of an oil. After half an hour, the oil was collected, washed with alkali, acid and water, and dried. The oil solidified after standing for a long time; weight 50 mg. A few milligrams of the ethyl ester of benzoylphenylalanylglycylglycine were obtained after numerous recrystallizations from aqueous alcohol; m.p. 151-152°. The compound gives an intense tripeptide biuret reaction and a negative ninhydrin reaction and does not contain free carboxyl. After hydrolysis, glycine and phenylalanine were detected on the chromatogram in phenol-water as solvents. Hydrolysis was effected with 20% HCl at 115° for 4 hours.

5. Reaction of O-hippuryl-N-benzoylserine with the ethyl ester of glycine. To a solution of 350 mg of O-hippuryl-N-benzoylserine in 2 ml of alcohol, neutralized with 1 N alkali, was added a solution of 750 mg of the ethyl ester of glycine hydrochloride in the equivalent quantity of 1 N alkali, 2 ml of phosphate buffer and (at pH 8) 2-3 mg of chymotrypsin. After 2 days, the transparent solution was evaporated to a small volume and the precipitate was filtered off and recrystallized from water. Yield of ethyl ester of benzoylglycylglycine 20 mg (15%); m.p. 113-115°.

A blank experiment was run under similar conditions. On evaporation of the solution the salt of O-hippuryl-N-benzoylserine with the ethyl ester of glycine was isolated. M.p. 151-153° (decomp.). The salt gave a positive reaction with ninhydrin.

6. Hydrolysis of N-benzoyl-O-peptides of serine by chymotrypsin. A weighed quantity of N-benzoyl-O-benzoylphenylalanylserine was dissolved in the minimum quantity of alcohol and the solution was neutralized with 0.1 N NaOH. Addition was then made of 2 ml of phosphate buffer and (at pH 8) of 2-3 mg of chymotrypsin. The pH was kept constant by addition of 0.1 N NaOH. Results of hydrolysis are shown in the diagram.

SUMMARY

It is shown that O-peptides of N-benzoylserine and of N-benzoylthreonine can serve as carriers of the amino acid residue in the fermentative synthesis of peptides. O-Peptides of N-benzoylserine and N-benzoylthreonine react with esters of amino acids and peptides under the action of chymotrypsin to give new N-peptides. O-Benzoylphenylalanyl-N-benzoylserine reacts with great ease.

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INVESTIGATION OF THE EXCHANGE REACTION OF OXY RADICALS WITH RADICALS OF ORGANOMAGNESIUM COMPOUNDS

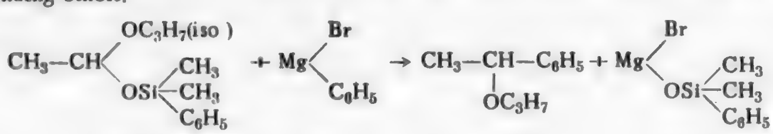
III. INTERACTION OF ORGANOMAGNESIUM COMPOUNDS WITH MIXED ORGANO-SILICON ACETALS

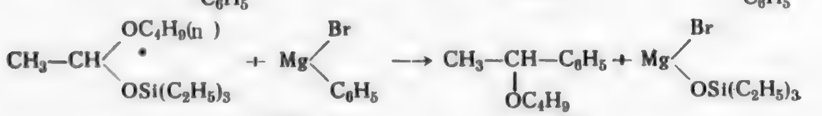
M. F. Shostakovskii, M. R. Kulibekov, and I. A. Shikhiev.

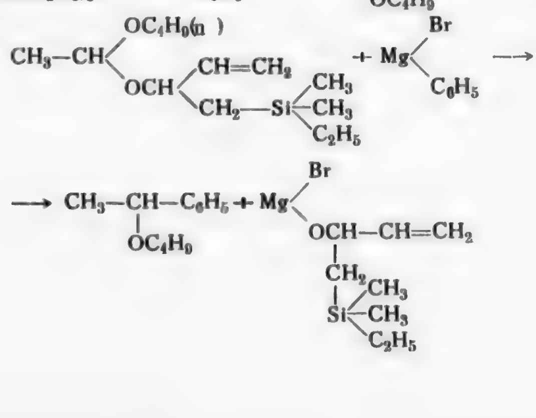
In the preceeding papers [1] we studied the action of a Grignard reagent on mixed and symmetrical organic acetals. It was found that in mixed acetals the heavy oxy radicals are the first to undergo exchange with the radical of the Grignard reagent with formation of the corresponding ethers. Concerning exchange of radicals in symmetrical acetals, we find the following sequence: OAr > OAlk > $OCH_2C_6H_5$. We attribute this pattern of exchange of oxy radicals by Grignard reagent radicals to a certain conjugation effect which causes one of the oxy radicals to become more labile.

It was of interest to investigate the analogous reaction of mixed organosilicon acetals [2] and to clarify the influence of silicon on the mobility of the oxy radicals in acetals. As we know, acetals of the aliphatic series easily undergo symmetrization, while fatty-aromatic acetals are not susceptible to this transformation and break down into vinyl alkyl ethers and phenol when heated. In this respect the mixed organosilicon acetals behave more like the alkyl-aryl acetals, and their symmetrization is accompanied by a series of other reactions. Like the alkyl-aryl acetals [3] they break down [4] when heated. The possibility of existence of mixed organosilicon acetals in two equilibrium forms has been demonstrated [5].

In the present work we studied the interaction of Grignard reagent with mixed organosilicon acetals and arrived at the conclusion that an oxy radical containing a silicon atom is susceptible to exchange regardless of whether the silicon atom is directly attached to oxygen or is in a more distant position. In both cases we obtained the corresponding ethers.

(I) 

(II) 

(III) 

The dimethylphenylsilanol and triethylsilanol formed under the reaction conditions dimerize with formation of the corresponding siloxanes. The alcohol (1-dimethylethylsilyl-3-buten-2-ol) obtained during reaction (III) does not dimerize. It should be noted that the oxy radical of isopropyldimethylphenylsilyl acetal (I) more easily enters into the exchange reaction than the oxy radical of butyltriethylsilyl acetal (II), and the latter more easily than the oxy radical of butyl-α-vinyl-β-dimethylethylsilylethyl acetal (III). These differences are evidently associated not only with the proximity of the silicon to the oxygen but with the presence of the phenyl radical.

We convey thanks to co-workers at the Institute of Organic Chemistry of the Academy of Sciences of the USSR, Kh. I. Kondrat'ev and S. I. Sadykh-zade, for kindly placing some of the starting substances at our disposal.

EXPERIMENTAL

1. Interaction of isopropyldimethylphenylsilyl acetal (I) with phenyl magnesium bromide. Phenyl magnesium bromide was prepared in the usual manner from 3 g of magnesium and 19 g of bromobenzene; the reflux condenser was thereupon replaced by a sloping condenser and the ether was distilled off. At 60° dropwise addition with stirring was commenced of the acetal (I) (11 g) with b.p. 111-111.5 (14 mm), n_D^{20} 1.4737, d_4^{20} 0.9410. The temperature rose sharply and at 90-100° the reaction mixture had changed into a brown suspension. After the whole quantity of acetal had been added, the reaction mixture was stirred for another hour and left overnight. The product was then decomposed with water acidified with acetic acid. The dark-brown oily layer was separated from the aqueous layer and treated with 10% hydrochloric acid (to hydrolyze the unreacted acetal); it was then washed and dried with sodium sulfate. Distillation in vacuo (2 mm) gave 4.6 g (60.68%) of substance with b. p. 68-70°, d_4^{20} 0.9149, n_D^{20} 1.4840; this was the isopropyl ether of phenyl sec. ethyl alcohol [6] Redistillation of the residue gave 3.2 g of bis-dimethylphenylsiloxane [7] with b.p. 112-113.5° (2 mm), d_4^{20} 0.9868 n_D^{20} 1.5177.

2. Reaction of butyltriethylsilyl acetal (II) with phenyl magnesium bromide. Phenyl magnesium bromide was prepared from 4 g of magnesium turnings and 26 g of bromobenzene. Dropwise addition of 20 g of (I) with b.p. 91-92° (10 mm), n_D^{22} 1.4266 to the Grignard reagent was made under the conditions of the preceding experiment. The temperature of the reaction mixture rose to 85° with progressive distillation of the ether. After the acetal had been added, the heated reaction mixture was stirred for another 2 hours. It should be noted that butyltriethylsilyl acetal enters less readily into exchange reaction than the preceding acetal under similar conditions. The product was decomposed with water and worked up as in the preceding experiment. Two distillations in vacuo gave 8.72 g (57.2%) of a substance with b.p. 80-82° (1 mm), d_4^{20} 0.9090, n_D^{20} 1.4822, which was the butyl ether of phenyl sec. ethyl alcohol [8]. From the residue was isolated 3.84 g of hexaethyldisiloxane with b.p. 130-132° (12 mm), d_4^{20} 0.8578, n_D^{20} 1.4329 [9].

3. Reaction of butyl-α-vinyl-β-dimethylethylsilylethyl acetal (III) with phenyl magnesium bromide. The starting (III) was prepared in 78.8% yield from vinyl butyl ether and 1-dimethylethylsilyl-3-buten-2-ol [10].

B.p. 94-94.5° (1 mm), n_D^{20} 1.4360, d_4^{20} 0.8545, MR_D 79.06; calculated 79.65.

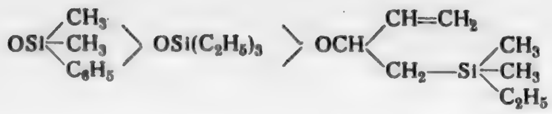
Phenyl magnesium bromide was prepared from 4 g of magnesium and 26 g of bromobenzene. 21 g of the organosilicon acetal was added dropwise at 105°. The reaction mass was heated (120°) with stirring for about 2 hours and left overnight. Appropriate working-up was followed by distillation in vacuo to give 3.45 g of dimethylethylsilyl-3-buten-2-ol [11], b.p. 48-49° (2 mm), n_D^{20} 1.4473, d_4^{20} 0.8555, and 7.7 g (53.14%) of phenyl sec. ethyl alcohol [8] with b.p. 78-80° (2 mm), d_4^{20} 0.9083, n_D^{20} 1.4865. Crystals of diphenyl separated out in the condenser.

SUMMARY

1. A study was made of exchange reactions of the oxy radicals of mixed organosilicon acetals with radicals of organomagnesium compounds.

2. It was shown that oxy radicals containing a silicon atom enter into exchange reactions.

3. It was established that such radicals exchange with Grignard radicals in the following order of facility:



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SYNTHESIS AND TRANSFORMATIONS OF BUTADIENYLSILANES

S. I. Sadykh-zade and A. D. Petrov

Butadienylsilanes or trialkylsilylbutadienes, like homologs of butadiene, can be synthesized with substituents located at the first or second carbon of the butadiene chain. The first representative of the trialkylsilylbutadiene series was prepared [1] by selective hydrogenation of trialkylsilylvinylacetylene:

$$R_3Si-C\equiv C-CH=CH_2 + H_2 \longrightarrow R_3Si-CH=CH-CH=CH_2$$

2-Trialkylsilylbutadiene was obtained [2] by the reaction scheme:

$$(C_2H_5)_3SiH + CH\equiv C-\overset{\overset{CH_3}{|}}{C}OH-CH_3 \longrightarrow CH_2=\overset{\overset{Si(C_2H_5)_3}{|}}{C}-\underset{\underset{CH_3}{|}}{C}OH-CH_3 \xrightarrow{-H_2O} CH_2=\underset{\underset{Si(C_2H_5)_3}{|}}{C}-\overset{\overset{CH_3}{|}}{C}=CH_2$$

In the present investigation, a short communication on which was recently published [3], we studied the synthesis of 1-trialkylsilylbutadienes according to the reaction steps:

$$-\!\!\!>Si-(CH_2)_nMgX + \overset{\overset{R}{|}}{C}H=CH-C\lessgtr^{O}_{H} \longrightarrow >Si-(CH_2)_n-CHOH-CH=CH-R \rightarrow$$
$$\xrightarrow{-H_2O} >Si-(CH_2)_{n-1}-CH=CH-CH=CH-R \quad (n=1,\ 3;\ R=H,\ CH_3,\ C_6H_5),$$

i.e., by dehydration of unsaturated organosilicon alcohols with an alcoholic group ether in the β- or δ-position. The method is interesting because it offers the possibility of synthesizing butadienylsilanes in which the silicon atom is at various distances from the butadiene chain. Judging by the data of Table 1, the yield of alcohols is little influenced by the character of the Grignard reagent or by the character of the radicals attached to the silicon atom. On the other hand, the yield of butadienylsilanes varied over extremely wide limits (Table 2). It was lower in the case of β-alcohols, and it fell by a factor of 2 to 2.5 in this series with progressive substitution of the methyl radical by ethyl, due to the secondary reaction of β-breakdown. It is interesting to note that in respect of β-breakdown these alcohols can be classed in two groups:

$$>Si-CH_2-CHOH-CH=CH_2 \text{ and } >Si-CH_2-CHOH-CH=CH-R.$$

Alcohols of the first group are dehydrated with little β-breakdown; alcohols of the second group with $R = CH_3$ are dehydrated with nearly quantitative β-breakdown; when $R = C_6H_5$, dehydration occurred even on simple distillation, as in the case of the saturated β-alcohol $>Si-CH_2-CHOH-CH_3$ studied by Whitmore [4]. This difference is accounted for by the influence of the substituent R on the direction of shift of the electrons. The effect is to increase the polarization and thereby to weaken the Si-C bond. This shift takes effect only along the system of conjugated bonds resulting from dehydration of the β-alcohols, and has no influence on the Si-C bond in the case of δ-alcohols, i.e. when the silicon atom is separated from the conjugated grouping by two carbons linked by a single bond. Thus, trialkyl-β-methylbutadienylethylsilane is found in 78% yield.

$$>Si-CH_2-CH_2-CH_2-CHOH-CH{=}CH-CH_3 \xrightarrow{-H_2O}$$
$$>Si-(CH_2)_2-CH{=}CH-CH{=}CH-CH_3$$

A study was made of the behavior of butadienylsilanes obtained by dehydration of β-alcohols in condensations with maleic anhydride, acrolein and acrylonitrile under the usual conditions of the Diels-Alder reaction. In all cases the reaction went with high yields of the corresponding products of synthesis. The cyclic aldehydes gave hydrazones with 2,4-dinitrophenylhydrazine. Hydrolysis of the maleic anhydride adduct gave a dibasic acid.

Dehydration of the β-alcohols gave the dimers in addition to the monomeric butadienylsilanes. The properties of these dimers, which are arbitrarily formulated as $[R_3Si\text{-}CH{=}CH\text{-}CH{=}CH_2]_2$, are presented in Table 2 (compound XVII-XIX). It should be noted that these properties did not alter when the dimers were boiled for several hours; they are apparently silicon-containing alkenylcyclohexenes (structural analogs of vinylcyclohexene), formed by cyclodimerization of butadiene. Boiling converts the monomeric butadienylsilanes both into dimers and higher molecular rubber-like polymers. Dehydration of δ-alcohols gives predominantly monomeric silicodiolefins in high yields; dimers are scarcely formed here – probably due to greater steric hindrance.

EXPERIMENTAL

We shall not describe the synthesis of the starting Grignard reagents* since it has already been described [5]. We give only the properties of methyldiethyl-γ-bromopropylsilane, which was prepared for the first time.**

B.p. 218° at 750 mm, n_D^{20} 1.4680, d_4^{20} 1.1039, MR_D 56.26; calculated 56.48.

Found %: C 43.35; H 8.56; Si 12.21; Br 34.41. $C_8H_{19}SiBr$. Calculated %: C 43.07; H 8.52; Si 21.56; Br 35.85.

1-Trimethylsilyl-3-buten-2-ol (I). 170 g of trimethyl-α-chloromethylsilane was added dropwise with cooling to 52.8g Mg in 700 ml of ether. To the Grignard reagent (cooled with ice) was added 123.2 g of freshly distilled acrolein with b.p. 51-52°. The reaction was violent and heat was released. After distillation of the ether, the product was fractionated at 24 mm. The following fractions were obtained: 1st, b.p. 35-70°, 20 g; 2nd, 70-75°, 160 g; the residue (40 g) decomposed when distilled.

Other secondary alcohols were obtained with use of crotonaldehyde under the same conditions as above: 1-dimethylethylsilyl-2-ol (II), 1-methyldiethylsilyl-3-buten-2-ol (III), 1-dimethylbutylsilyl-3-buten-2-ol (IV), 1-triethylsilyl-3-buten-2-ol (V), 1-dimethylethylsilyl-3-penten-2-ol (VI), 1-trimethylsilyl-5-hexen-4-ol (VII), 1-methyldiethylsilyl-5-hexen-4-ol (VIII), and 1-methyldiethylsilyl-5-hepten-4-ol (IX) (properties and yields are given in Table 1).

We shall consider in more detail the products of synthesis of 1-methyldiethylsilyl-5-hexen-4-ol (VIII), obtained by us in quantity of 180 g. They were fractionated at 2 mm to give: 1st fraction, 30-94°, 20 g; 2nd fraction, 94-97°, 110 g; 3rd fraction, 97-150°, 21 g; the residue of 17 g did not distill without decomposition. Redistillation in a column gave, apart from the secondary alcohol, by-products of the reaction. Methyldiethylpropylsilane, for example, was isolated from the 1st fraction:

B.p. 143.5°, n_D^{20} 1.4252, d_4^{20} 0.7619, MR_D 48.45; calculated 48.80.

Found %: C 66.64; H 13.90; Si 19.10. $C_8H_{20}Si$. Calculated %: C 66.70; H 13.90; Si 19.44.

The 3rd fraction yielded a substance with b.p. 127.5-129° at 2 mm, identified as 1,6-bis-methyldiethylsilylhexane:***

n_D^{20} 1.4568, d_4^{20} 0.8502, MR_D 91.77; calculated 92.09.

Found %: C 66.80; H 13.04. $C_{16}H_{38}Si$. Calculated %: C 67.13; H 13.3.

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*I. Avgushevich [3] participated in the synthesis of α-chloromethyltrialkylsilanes.

** $(CH_3)(C_2H_5)SiCH_2CH_2CH_2Br$.

*** $(CH_3)(C_2H_5)Si(CH_2)_6Si(C_2H_5)_2(CH_3)$.

TABLE 1

Compound No.	Compound	Boiling point (pressure in mm)		n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Yield (in %)	Found (%) C	Found (%) H	Found (%) OH	Found (%) Si	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) OH	Calculated (%) Si
I	$(CH_3)_3Si-CH_2-CHOH-CH=CH_2$ 1-Trimethylsilyl-3-buten-2-ol	70–70.5	(24)	1.4427	0.8427	45.06	45.25	50.5	57.45, 57.25	11.10, 11.05	1.1, 0.87	19.15, 18.84	$C_7H_{16}OSi$	58.27	11.17	1.0	19.45
II	$(CH_3)_2(C_2H_5)Si-CH_2-CHOH-CH=CH_2$ 1-Dimethylethylsilyl-3-buten-2-ol	74–75	(9)	1.4492	0.8528	49.81	49.88	68.7	60.20, 60.09	11.42, 11.41	0.96, 1.04	17.65, 17.69	$C_8H_{18}OSi$	60.70	11.46	1.0	17.72
III	$(CH_3)(C_2H_5)_2Si-CH_2-CHOH-CH=CH_2$ 1-Methyldiethylsilyl-3-buten-2-ol	79–80	(6)	1.4611	0.8651	54.57	54.51	51.5	62.24, 62.16	11.48, 31.68	0.888, 1.050	16.53, 16.48	$C_9H_{20}OSi$	62.72	11.69	1.0	16.28
IV	$(CH_3)_2(C_4H_9)Si-CH_2-CHOH-CH=CH_2$ 1-Dimethylbutylsilyl-3-buten-2-ol	75–76	(2.5)	1.4548	0.8501	59.40	59.14	64.7		—	0.915, 1.15	15.76, 15.32	$C_9H_{20}OSi$		—	1.0	15.10
V	$(C_2H_5)_3Si-CH_2-CHOH-CH=CH_2$ 1-Triethylsilyl-3-buten-2-ol	76–77	(2)	1.4648	0.8816	58.41	59.14	53.6	—	—	0.927	—	$C_{10}H_{22}OSi$	—	—	1.0	—
VI	$(CH_3)_2(C_2H_5)Si-CH_2-CHOH-CH=CHCH_3$ 1-Dimethylethylsilyl-3-penten-2-ol	70–71	(3)	1.4583	0.8566	54.51	54.91	54.4	—	—	1.19, 0.958	—	$C_9H_{20}OSi$	—	—	1.0	—
VII	$(CH_3)_3Si-(CH_2)_3-CHOH-CH=CH_2$ 1-Trimethylsilyl-5-hexen-4-ol	70–71	(3)	1.4422	0.8352	54.62	54.51	80.0	62.32, 62.30	12.20, 12.30	—	17.17	$C_{11}H_{24}OSi$	62.66	11.80	—	16.37
VIII	$(CH_3)(C_2H_5)_2Si-(CH_2)_3-CHOH-CH=CH_2$ 1-Methyldiethylsilyl-5-hexen-4-ol	87–87.5	(1)	1.4570	0.8648	63.11	63.77	64.0	—	—	—	14.56	$C_{11}H_{24}OSi$	—	—	—	14.02
IX	$(CH_3)(C_2H_5)_2Si-(CH_2)_3-CHOH-CH=CH-CH_3$ 1-Methyldiethylsilyl-5-hepten-4-ol	102.0	(1)	1.4605	0.8653	67.93	68.40	70.0	67.40, 67.60	12.40, 12.23	—	12.66, 12.82	$C_{12}H_{26}OSi$	67.22	12.22	—	13.10

Consequently, the halide, in which the silicon is in the γ-position to the halogen and no longer exerts an influence on the latter, reacts with aldehydes in a similar manner to silicon-free RMgX to form by-products R-R and R-H (compare [6]) in addition to the main product — the secondary alcohol. Allyl alcohol was presumably also formed here and came over with the ether.

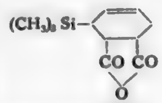
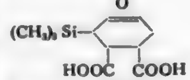
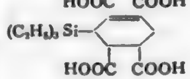
1-Trimethylsilylbutadiene (X). 0.5 g of $KHSO_4$ was added every 15 minutes to 144 g of 1-trimethylsilyl-3-buten-2-ol (I) in a flask fitted with a column. After 2-hours' heating on a water bath, the operation was completed. After separation of the water, the product of dehydration was washed with 3% Na_2CO_3 and dried with Na_2SO_4. It was fractionated in a column at atmospheric pressure with addition of hydroquinone. The following fractions were obtained: 1st, to 98.5°, 4 g; 2nd, 98.5-99°, 25 g; 3rd, 99-113.5°, 4 g; 4th, 113.5°, 50 g; residue 13 g. The product of β-decomposition $(CH_3)_3SiOSi(CH_3)_3$ was identified in the 2nd fraction. The 4th fraction contained 1-trimethylsilylbutadiene (X). Redistillation of the residue at 3 mm gave a dimer with b.p. 95°. The residue from the redistillation was a soluble and fusible polymer. Under similar conditions we prepared 1-dimethylethylsilylbutadiene (XI), 1-methyldiethylsilylbutadiene (XII), and 1-triethylsilylbutadiene (XIII). Yield and analytical results are presented in Table 2.

1-Trimethylsilyl-3,5-hexadiene (XIV). 50 g of 1-trimethylsilyl-5-hexen-4-ol (VII) and a few drops of concentrated H_2SO_4 were put into a flask fitted with a reflux condenser. The mixture was heated for 1 hour at 100-115°. The water was separated, and the product was dried and fractionated to give the diolefinic silicohydrocarbon b.p. 162-162.5°, weight 34 g. The same conditions were employed in the preparation of 1-methyldiethylsilyl-3,5-hexadiene (XV) and 1-methyldiethylsilyl-3,5-heptadiene (XVI)(see Table 2 for properties and analytical data).

Adduct with maleic anhydride (XX). 2 g of maleic anhydride and 1.5 g of trimethylbutadienylsilane were heated for 30 minutes at 100-115°. After cooling, the mixture was poured into a beaker of water. The crystals were washed with water and recrystallized from acetone and ligroine. M.p. 116°. The adduct with triethylbutadienylsilane had m.p. 124.5°. Boiling with water converted the adducts into dibasic acids (Table 2, compounds XXI and XXII).

1-Trimethylsilyl-5-nitrilo-2-cyclohexene. A 100-ml ampoule containing 12.6 g of trimethyl-

TABLE 2

Compound No.	Compound	B.p. (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Выход (в %)	Found (%) C	Found (%) H	Found (%) Si	Empirical formula	Calculated (%) C	Calculated (%) H	Calculated (%) Si
(X)	$(CH_3)_3Si-CH=CH-CH=CH_2$ 1-Trimethylsilylbutadiene	113.5° (759)	1.4480	0.7538	44.84	43.23	40	65.54, 65.44	11.34 11.59	22.38 22.13	$C_7H_{14}Si$	66.51	11.11	22.19
(XI)	$(CH_3)_2(C_2H_5)Si-CH=CH-CH=CH_2$ 1-Dimethylethylsilylbutadiene	138–138.5 (751)	1.4490	0.7695	48.89	47.86	35	67.97 68.15	11.72 11.86	19.61 19.68	$C_8H_{16}Si$	68.51	11.49	20.0
(XII)	$(CH_3)(C_2H_5)_2Si-CH=CH-CH=CH_2$ 1-Methyldiethylsilylbutadiene	162–162.5 (752)	1.4585	0.7876	53.5	52.49	17.3	69.25 69.28	12.00 11.90	17.78 18.03	$C_9H_{18}Si$	70.05	11.69	18.18
(XIII)	$(C_2H_5)_3Si-CH=CH-CH=CH_2$ 1-Triethylsilylbutadiene	184.5–185 (755)	1.4695	0.8070	58.15	57.12	15.0	71.30 71.00	12.50 12.45	16.10 16.23	$C_{10}H_{20}Si$	71.34	11.98	16.68
(XIV)	$(CH_3)_3Si-CH_2-CH_2-CH=CH-CH=CH_2$ 1-Trimethylsilyl-3,5-hexadiene	162.5 (749)	1.4515	0.7777	53.47	52.49	18.0	69.50 69.40	12.50 12.62	18.36 18.35	$C_9H_{18}Si$	70.05	11.69	18.18
(XV)	$(CH_3)(C_2H_5)_2Si-CH_2-CH_2-CH=CH-CH=CH_2$ 1-Methyldiethylsilyl-3,5-hexadiene	78–79 (5.5)	1.4648	0.8130	62.08	61.75	30 *	—	—	15.10 15.19	$C_{11}H_{22}Si$	—	—	15.37
(XVI)	$(CH_3)(C_2H_5)_2Si-CH_2-CH_2-CH=CH-CH=CH-CH_3$ 1-Methyldiethylsilyl-3,5-heptadiene	75–75.5 (1)	1.4740	0.8127	67.92	66.38	79	73.30 73.45	12.57 12.60	13.50 13.48	$C_{12}H_{24}Si$	73.36	12.32	14.27
(XVII)	$[(CH_3)_3Si-CH=CH-CH=CH_2]_2$	95 (3.5)	1.4790	0.8640	82.84	83.14	2.5	65.71 65.87	11.19 11.07	21.74 21.46	$C_{14}H_{28}Si_2$	66.51	11.11	22.19
(XVIII)	$[(CH_3)_2(C_2H_5)Si-CH=CH-CH=CH_2]_2$	117–118 (2.5)	1.4830	0.8635	92.72	92.40	10	67.67 67.77	11.41 11.42	19.67 19.73	$C_{16}H_{32}Si_2$	68.51	11.49	20.00
(XIX)	$[(CH_3)(C_2H_5)_2Si-CH=CH-CH=CH_2]_2$	139–141 (3)	1.4930	0.8849	101.65	101.65	16	69.33 70.19	12.04 12.09	17.36 17.38	$C_{18}H_{36}Si_2$	70.05	11.69	18.18
(XX)		124.5 **	—	—	—	—	—	59.00 58.77	7.00 7.24	12.31 12.26	$C_{11}H_{10}O_3Si$	58.93	7.14	12.50
(XXI)		103.0 **	—	—	—	—	—	—	—	11.51 11.21	$C_{11}H_{18}O_4Si$	—	—	11.57
(XXII)		131–132 **	—	—	—	—	—	59.42 59.50	8.77 8.67	8.99 9.56	$C_{14}H_{24}O_4Si$	59.12	8.50	9.87

* Part of the product polymerized.

** Melting point.

silylbutadiene, 8 g of acrolein and a crystal of iodine was sealed and heated to 190-210° for 3 hours. Distillation at 2 mm gave 12 g of liquid reaction product which was easily mobile and had a pleasant odor. B.p. 78-78.5°, d_4^{20} 0.9272, n_D^{20} 1.4820.

Found %: C 66.94; H 9.71; Si 15.60. $C_{10}H_{17}NSi$. Calculated %: C 67.07; H 9.47; Si 15.64.

1-Dimethylethylsilyl-5-carbomethoxy-2-cyclohexene. An ampoule containing 14 g of dimethylethylbutadienylsilane and 12.9 g of freshly distilled methyl acrylate was heated under the preceding conditions to give (distillation at 4 mm) 16 g of product with b.p. 83-84°, n_D^{20} 1.4808, d_4^{20} 0.9865.

Found %: Si 12.57. $C_{12}H_{22}O_2Si$. Calculated %: Si 12.39.

1-Methyldiethylsilyl-2-cyclohexen-5-al. An ampoule containing 10 g of methyldiethylbutadienylsilane and 5 g of freshly distilled acrolein was heated at 170-190° for 1 hour. 5 g of product was isolated by distillation at 2 mm; b.p. 102-103°, n_D^{20} 1.4918, d_4^{20} 0.9518.

Found %: C 68.40; H 10.75. $C_{12}H_{22}OSi$. Calculated %: C 68.49; H 10.54.

The 2,4-dinitrophenylhydrazone of this aldehyde had m.p. 121.0°.

Found %: N 14.56. $C_{18}H_{26}O_4N_4Si$. Calculated %: N 14.35.

1-Triethylsilyl-2-cyclohexen-5-al was synthesized under similar conditions: b.p. 114.5-115.5° at 2 mm, n_D^{20} 1.4955, d_4^{20} 0.9560.

Found %: C 69.54; H 10.10. $C_{13}H_{24}OSi$. Calculated %: C 69.55; H 10.79.

SUMMARY

1. It is shown that unsaturated β- and γ-silicoorganic alcohols can be synthesized by condensation of Grignard reagents from α- and γ-silicohalides with acrolein and crotonaldehyde. It was established that dehydration of the β-derivatives proceeds with partial β-breakdown (the extent of which is governed by the structure of the alcohol), as well as with secondary formation of dimers and monomers. The γ-alcohols are dehydrated without degradation and without formation of dimers.

2. Butadienylsilanes were subjected to Diels-Alder condensation with acrolein, acrylic ester, acrylonitrile and maleic anhydride.

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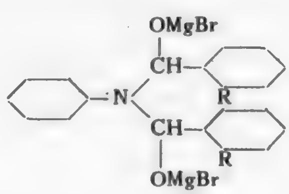
REACTIONS OF MAGNESYLAMINES

VI. STERIC HINDRANCE IN THE ARAMIDATION OF AROMATIC ALDEHYDES WITH THE HELP OF N,N'-bis-(HALOMAGNESIUM)ARYLAMINES

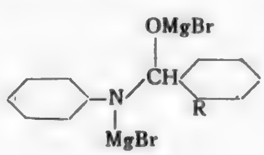
P. A. Petinunin and L. A. Tetiueva

In order to clarify the influence of steric hindrance during amidation of aromatic aldehydes with the help of dimagnesylamines, we ran a series of experiments with aldehydes and amines containing various substituents in the ortho-position. The experiments showed that aldehydes and dimagnesylamines exert steric hindrance to different degrees. Aldehydes are characterized by greater steric hindrance. Introduction of one substituent in the ortho-position, for example, blocks the aldehyde group to such a extent that the aramidation of such aldehydes becomes substantially impossible. This was demonstrated in the reaction between o-toluidine and o-methoxybenzaldehyde on the one hand and N,N'-bis-(bromomagnesium)aniline on the other. Experiments were performed in pyridine solution with a heating period of one hour. Heat was developed when the reactants were stirred, but the original substances were recovered unchanged after decomposition of the reaction mass with dilute hydrochloric acid.

On the basis of our proposed reaction mechanism [1], disproportionation can proceed only in the complex (I), which is formed by reaction of two molecules of aldehyde with one molecule of magnesylamine



(I)

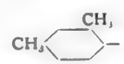
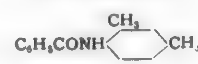
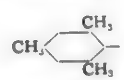
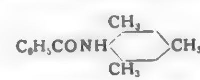
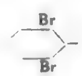
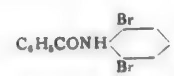
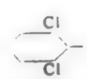
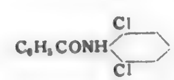


(II)

$R = CH_3, CH_3O$.

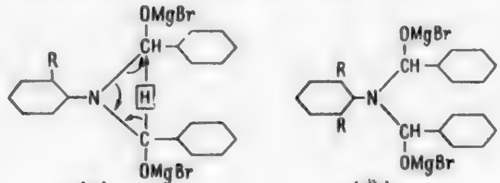
Disproportionation of the above aldehydes does not occur, and consequently the complex (I) is not formed, the process stopping with formation of complex (II). Complex (I) might have been formed by interaction of (II) with a fresh molecule of aldehyde. This is prevented, however, by steric hindrances which are simultaneously exerted both by (II) and by the aldehyde due to the substituent in the ortho-position.

Steric hindrance by N,N'-bis-(bromomagnesium)arylamines was established by experiments between dimagnesylamines containing substituents in the ortho-position and aldehydes without substituents in that position. Experiments were carried out in a medium of ether or pyridine. Results are presented in the table. We see from the results that the reaction is not appreciably inhibited by dimagnesylamines containing one substituent (Br, Cl, CH_3, OCH_3) in the ortho-position (experiments 1-6). The yields of the corresponding arylamides are approximately the same as in the case of dimagnesylamines without substituents in the ortho-position, namely: 14-19% in the ether medium and 45-75% in the pyridine medium. These results demonstrate that the presence of one substituent in the ortho-position to the $(BrMg)_2N$ group does not hinder formation of the complex (III), and disproportionation to this complex proceeds normally. A different picture is obtained when experiments are run with dimagnesylamines in which both of the ortho-positions to the $(BrMg)_2N$ group are occupied by sub-

Expt. No.	Aldehyde	Nature of Ar in $ArN(MgBr)_2$	Product of reaction *	Yield (in %)	Melting point	
					our data	literature [2]
1	C_6H_5CHO	o-BrC_6H_4—	$C_6H_5CONHC_6H_4Br$-o	15.6	105—107°	116°
2	C_6H_5CHO	o-ClC_6H_4—	$C_6H_5CONHC_6H_4Cl$-o	18.9	100—101	99—101
3	C_6H_5CHO	o-$CH_3C_6H_4$—	$C_6H_5CONHC_6H_4CH_3$-o	14.3	142—143.5	143
4	C_6H_5CHO			44.5	192	192
5	p-BrC_6H_4CHO	o-$CH_3C_6H_4$—	p-$BrC_6H_4CONHC_6H_4CH_3$-o (IV)	74.58	158—159	—
6	p-BrC_6H_4CHO	o-$CH_3OC_6H_4$—	p-$BrC_6H_4CONHC_6H_4OCH_3$-o (V)	70.68	136—137.5	—
7	C_6H_5CHO			13.4	204	204
8	C_6H_5CHO		 (VI)	0.56	177—178	—
9	C_6H_5CHO		 (VII)	0.75	158—159	—

* Ether was the solvent in experiments 1-3, 8 and 9, and pyridine in experiments 4-7.

stituents (experiments 7-9). No heat is developed when benzaldehyde is added to ether solutions of dimagnesylamines prepared from 2,6-dichloro- and 2,6-dibromoanilines. The yields of the corresponding arylamides were negligible. Slightly better results were obtained in a medium of pyridine. The mesidide of benzoic acid, for example, was obtained in a yield of 13.4% (experiment 7). But even this yield is more than 3 times smaller than that for dimagnesylamines without substituents in the ortho-position. Just as in the case of aldehydes, the steric hindrance manifested by dimagnesylamines with substituents in both of the ortho-positions hinders formation of the complex (VIII) in which an oxidation-reduction must take place. Here again the reaction is evidently limited in the main by the equimolar reaction of the starting substances.



(III) R = Br, Cl, CH_3, CH_3O.

(VIII) R = Cl, Br, CH_3.

EXPERIMENTAL

The procedures were the same as those described in the preceding communications. In one experiment 0.0125 mole of N,N'-bis-(bromomagnesium)arylamine was reacted with 0.025 mole of aromatic aldehyde. Arylamides (VI) and (VII) were identified in mixed melting point tests with substances obtained by reaction of ethyl benzoate with dimagnesylamines from 2,6-dibromo- and 2,6-dichloroanilines.

o-Toluidide of p-bromobenzoic acid (IV). Sparingly soluble in ether, more easily soluble in alcohol, toluene, chloroform and acetone. Crystallizes from glacial acetic acid in the form of colorless plates.

The melting points of this compound and of the other newly prepared substances are listed in the table.

Found %: N 4.99, 4.67. $C_{14}H_{12}ONBr$. Calculated %: N 4.83.

o-Anisidide of p-bromobenzoic acid (V). Sparingly soluble in ether, and readily soluble in alcohol, acetic acid, benzene and chloroform. Crystallizes from glacial acetic acid in the form of colorless rodlets.

Found %: N 4.42, 4.50. $C_{14}H_{12}O_2NBr$. Calculated %: N 4.57.

2,6-Dibromoanilide of benzoic acid (VI). Sparingly soluble in ether, readily soluble in acetic acid, alcohol, benzene and acetone. Prisms (from alcohol). Obtained in 75.8% yield by reaction of ethyl benzoate with N,N'-bis-(bromomagnesium)-2-6-dibromoaniline in 1 : 1 ratio. No depression of melting point in a mixed test.

Found %: N 3.84, 3.95, $C_{13}H_9ONBr_2$. Calculated %: N 3.94.

2,6-Dichloroanilide of benzoic acid (VII). Sparingly soluble in ether, readily soluble in acetic acid, benzene, alcohol and acetone. Prisms (from alcohol). Prepared in 75.2% yield by reaction of equimolar amounts of ethyl benzoate and N,N'-bis-(bromomagnesium)-2,6-dichloroaniline. No depression of melting poin in a mixed test.

Found %: N 5.15, 5.19. $C_{13}H_9ONCl_2$. Calculated %: N 5.26.

SUMMARY

1. A study was made of steric hindrance in the aramidation of aromatic aldehydes with the help of N,N'-bis-(halomagnesium)arylamines.

2. It was established that the strongest steric hindrance is exerted by the aldehyde: one substituent in the ortho-position to the aldehyde group substantially rules out the possibility of aramidation.

3. N,N'-bis-(halomagnesium)arylamines exert steric hindrance when both of the ortho-positions relative to the $(BrMg)_2N$ group are occupied by substituents.

4. A previously undescribed series of arylamides was prepared and their properties were studied.

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SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

VII. OXIDATIVE CHLOROPHOSPHONATION BY MEANS OF ALKYL AND DIALKYLAMIDOPHOSPHORODICHLORIDITES *

Iu. M. Zinov'ev, V. N. Kulakova and L. Z. Soborovskii

Oxidative chlorophosphonation of hydrocarbons and their derivatives had been accomplished previously by means of phosphorus trichloride, alkyldichlorophosphines and aryldichlorophosphines [1]. It has been shown in the present work that one may use alkyl phosphorodichloridites (alkyl dichlorophosphites) and dialkylamidophosphorodichloridites (dialkylaminodichlorophosphines), i.e. compounds in which the hydrocarbon residue is bound to the phosphorus atom through a third element: $RH + 2\ R'XPCl_2 + O_2 \rightarrow RP(O)(XR')Cl + R'XP(O)Cl_2 + HCl$, where R and R' are hydrocarbon radicals and X is oxygen or nitrogen, as the phosphonating agent. We performed the oxidative chlorophosphonation of cyclohexane (with ethyl phosphorodichloridite) and of vinyl chloride (with methyl phosphorodichloridite and dimethylamidophosphordichloridite) with these reagents. As the result of these reactions there were isolated the corresponding phosphonic chlorides which contain the phosphorus-carbon bond.

Oxidative chlorophosphonation of cyclohexane with ethyl phosphorodichloridite led to formation of a mixture of compounds, the separation of which by fractionation turned out to be difficult. Therefore, in order to prove the course of the reaction in accord with the scheme shown above, i.e. to prove the formation of a carbon-phosphorus bond, we treated the resulting mass with water and, from the hydrolysis products, we isolated a substance shown to be cyclohexanephosphonic acid (cyclohexylphosphonic acid).

Oxidative chlorophosphonation of compounds of the ethylene series by alkyl phosphorodichloridites proceeds completely analogously to the reaction which is performed with phosphorus trichloride. This reaction was run with vinyl chloride. Methyl phosphorodichloridite and dimethylamidophosphorodichloridite were used as the phosphonating agents. From the products of the reaction of vinyl chloride and methyl phosphorodichloridite there was isolated a fraction which boiled at 105-115° (5 mm), the main bulk of which consisted of methyl dichloroethylphosphonochloridate. We failed to isolate this compound in the pure state owing to the instability of substances of this type. However, the formation of phosphorus-carbon bond was proved by the preparation from this fraction of the dimethyl ester of dichloroethylphosphonic acid, identical in its properties with a specimen prepared from the previously described chloride of dichloroethylphosphonic acid [2].

$$CH_2{=}CHCl + 2CH_3OPCl_2 + O_2 \longrightarrow C_2H_3Cl_2P(O)(OCH_3)Cl + CH_3OP(O)Cl_2$$
$$C_2H_3Cl_2P(O)(OCH_3)Cl + CH_3OH \longrightarrow C_2H_3Cl_2P(O)(OCH_3)_2 + HCl$$

Oxidative chlorophosphonation of vinyl chloride by dimethylamidophosphorodichloridite proceeds according to the following scheme:

$$CH_2{=}CHCl + 2(CH_3)_2NPCl_2 + O_2 \longrightarrow C_2H_3Cl_2P(O)[N(CH_3)_2]Cl + (CH_3)_2NP(O)Cl_2$$

* Alkyl and dialkylphosphoramidous dichlorides.

Ethyl ester of N,N-dimethyl-dichloroethylphosphonamidic acid was prepared from the resulting choride of N,N-dimethyl-dichloroethylphosphonamidic acid and sodium ethoxide.

It had been shown previously that oxidative chorophosphonation of vinyl chloride with phosphorus trichloride leads to the formation of two isomeric chlorides of dichloroethylphosphonic acid [2]. The compounds prepared from vinyl chloride in the present work are also evidently isomer mixtures the structures of which may be expressed by the formulas $ClCH_2CHClP(O)(OCH_3)Cl$ and $CHCl_2CH_2P(O)(OCH_3)Cl$ (for products of oxidative chlorophosphonation with methyl phosphorodichloridite) and $ClCH_2CHClP(O)[N(CH_3)_2]Cl$ and $CHCl_2CH_2P(O)[N(CH_3)_2]Cl$ (for the chloride synthesized from dimethylamidophosphorodichloridite). We did not accomplish the isolation of the individual isomers.

EXPERIMENTAL

1. Oxidative chlorophosphonation of cyclohexane by ethyl phosphorodichloridite. Oxygen was passed through a mixture of 21 g (0.25 mole) of cyclohexane and 180 g. (1.2 moles of ethyl phosphorodichloridite until the reaction ceased. From the reaction mixutre there was isolated 11 g of a fraction which boiled in the interval of 106-112° (3 mm); d_4^{20} 1.2576. The substance passed almost completely into solution on being warmed with thirty ml of water. After the removal of water, crystals were isolated and these were recrystallized from alcohol [m. p. 160-161°]. Cyclohexylphosphonic acid, prepared from the acid chloride synthesized by oxidative chlorophosphonation of cyclohexane by phosphorus trichloride, melted at 162°. The mixed melting point of the two specimens was 161-162°.

Found %: C 44.37, 44.62; H 8.68, 8.71; P 19.47, 19.57. $C_6H_{13}O_3P$. Calculated %: C 43.94; H 8.00; P 18.87.

2. Oxidative chlorophosphonation of vinyl chloride by methyl phosphorodichloridite. a) Oxygen was passed through 200 g of vinyl chloride and 128.2 g (0.96 mole) of methyl phosphorodichloridite at −20° until the reaction ceased. After the removal of low-boiling products, there was distilled 25 g. (12.3%) of a substance boiling at 110-118° (5 mm). The distillation was accompanied by partial decomposition. After a second distillation there was isolated the fraction with b.p. 105-110° (5 mm); d_4^{20} 1.5220; n_D^{20} 1.4693.

Found %: P 14.26, 14.24. $C_3H_6O_2PCl_3$. Calculated %: P 14.65.

b) Eighteen and a half grams of the substance prepared as described above was added dropwise at 10° to 100 ml. of methanol. From the reaction mixture there was isolated 14.5 g. of a substance with b.p. 105-109° (4 mm); d_4^{20} 1.4060; n_D^{20} 1.4508.

c) To 48 g (1.5 moles) of methanol there was added dropwise at −10° 21.6 g (0.1 mole) of dichloroethylphosphonic dichloride.* From the reaction mixture there was isolated a substance boiling at 110-112° (4 mm); d_4^{20} 1.4039; n_D^{20} 1.4510. The yield: 18.1 g (87.5%).

Found %: C 23.26, 23.32; H 4.76, 4.51; P 14.82, 14.34; M 213.5. $C_4H_9OPCl_2$. Calculated %: C 23.20; H 4.38; P 14.96. M 207.01.

3. Oxidative chlorophosphonation of vinyl chloride by dimethylamidophosphorodichloridite: a) Oxygen was passed at −30° through a mixture of 90 g (1.44 moles) of vinyl chloride and 82 g (0.56 mole) of dimethylamidophosphorodichloridite (b.p. 146-148°, d_4^{20} 1.2624; according to data from [3]: b.p. 40° at 10 mm. d_4^{20} 1.2644) until the reaction ceased. Seventy two grams of unreacted vinyl chloride was isolated from the reaction mixture along with 30.2 g of dimethylamide of phosphorodichloridic acid and 14.4 g (23%) of a substance which boiled, after two distillations, at 114-115° (1.5 mm); d_4^{20} 1.4036; n_D^{20} 1.4780.

Found %: C 20.25, 20.50; H 4.03, 4.04; N 6.73, 6.41. $C_4H_9ONPCl_3$. Calculated %: C 21.40; H 4.04; N 6.23.

b) The chloride of N,N-dimethyl-dichloroethylphosphonamidic acid, prepared from the chloride of dichloroethylphosphonic acid [2] and dimethylamine, boiled at 118° (2.5 mm); d_4^{20} 1.3997; n_D^{20} 1.4775.

* Prepared by oxidative chlorophosphonation of vinyl chloride with phosphorus trichloride [2].

4. Preparation of the ethyl ester of N,N-dimethyl-dichloroethylphosphonamidic acid. To the solution of 7.1 g (0.035 mole) of the chloride of N,N-dimethyl-dichloroethylphosphonamidic acid in 50 ml of dry ether. there was added 2.4 g (0.035 mole) of sodium ethoxide in 20 ml of ether. Five ml of water was added to the reaction mixture to dissolve the precipitated salt. There was isolated 1.4 g (17%) of the substance with:

B.p. 85-90° ($1 \cdot 10^{-5}$ mm); d_4^{20} 1.2191; n_D^{20} 1.4495; MR_D 51.83; calculated MR_D 51.80.

Found %: C_2H_5O 18.48, 1819. $C_6H_{14}O_2Cl_2NP$. Calculated %: C_2H_5O 19.25.

SUMMARY

1. It has been shown that in oxidative chlorophosphonation of hydrocarbons and their derivatives one may employ as phosphonating agents the products of replacement of chlorine in phosphorus trichloride, these having the type $RXPCl_2$, where the hydrocarbon residue is bound to the phosphorus atom by a third element X.

2. Oxidative chlorophosphonation of cyclohexane by ethyl phosphorodichloridite and of vinyl chloride by methyl phosphorodichloridite and dimethylaminophosphorodichloridite was realized.

3. The chloride and the ethyl ester of N,N-dimethylamido-dichloroethylphosphonamidic acid, dimethyl ester of dichloroethylphosphonic acid and methyl ester of dichloroethylphosphonochloridic acid have been synthesized.

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* Original Russian pagination. See C. B. Translation.

TETRAACYLOXYSILANES IN ORGANIC SYNTHESIS

XV. SYNTHESIS OF α, β-UNSATURATED ACIDS OF THE FURAN AND THIOPHENE SERIES

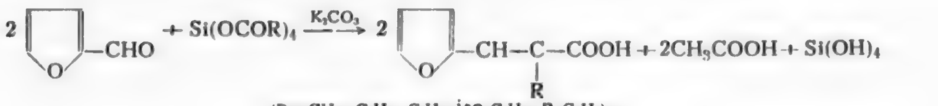
Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov

In our previous work [1] we showed that in the synthesis of cinnamic acid and its homologs (α-alkyl-β-phenylacrylic acids) by the Perkin reaction the silicoanhydrides of saturated monobasic acids (tetraacyloxysilanes) can successfully take the place of acid anhydrides in the condensation with benzaldehyde. It was therefore of interest to condense tetraacyloxysilanes with other aldehydes with an aromatic character – furfural and thiophene-2-aldehyde – in order to prepare β-(furyl-2)- and β-(thienyl-2)-acrylic acids.

According to the data of Marckwald [2] β-(furyl-2)-acrylic acid is obtained in good yield (80%) by the normal Perkin reaction from furfural and acetic anhydride in presence of potassium acetate.

The literature contains no information about the preparation of α-methyl-α-propyl- and α-butyl-β-(furyl-2)-acrylic acids by the Perkin reaction. Baeyer [3] and Carter [4] obtained α-ethyl-β-(furyl-2)-acrylic acid in 80% yield by condensation of furfural with butyric anhydride in presence of sodium butyrate. Schaarschmidt and co-workers [5] only obtained a negligible yield of α-isopropyl-β-(furyl-2)-acrylic acid (0.5%) on condensing furfural with isovaleric anhydride in presence of sodium isovalerate. Their main product (45%) was 3-methyl-1-(furyl-2)-1-butene (furylisoamylene), apparently the result of decarboxylation of the intermediate product of condensation as in the analogous condensation with benzaldehyde [6].

In the present work we studied the condensation of furfural with silicoanhydrides of acetic, propionic, butyric, valeric, isovaleric and caproic acids and we obtained β-(furyl-2)acrylic and (respectively) α-methyl-, α-ethyl, α-propyl-, α-isopropyl- and α-butyl-β-(furyl-2)-acrylic acids, thereby demonstrating that the field of application of tetraacyloxysilanes in organic synthesis can be still further widened.



($R = CH_3$, C_2H_5, C_3H_7, iso-C_3H_7, n-C_4H_9).

Condensation of furfural with silicoacetic anhydride proceeds best of all in presence of potassium acetate, and the maximum yield of β-(furyl-2)-acrylic acid (59%) is reached with a molar ratio of components equal to 1 : 1.2 : 1 and with 10-hours' heating at 150-155°; the yield of acid fell to 53% when the heating period was reduced to 5 hours; prolongation of the heating period to 15 hours led to greater resinification and to a fall in yield of the acid to 45%. The acid yield was 52% when heating at 180° was carried out for 3 hours. The yield did not exceed 26% if postassium carbonate was used as condensing agent.

On the other hand, the condensation of furfural with silicoanhydrides of propionic and butyric acids in presence of potassium carbonate led to yields of 70.5% of α-methyl-β-(furyl-2)-acrylic acid and 60% of α-ethyl-β-(furyl-2)-acrylic acid respectively. Condensation of furfural with silicoanhydrides of valeric and caproic acids gave α-propyl and α-butyl-β-(furyl-2)-acrylic acids in the lower yields of 33 and 26% respectively. A very low yield of α-isopropyl-β-(furyl-2)-acrylic acid (3.3%) resulted from condensation of furfural with silicoisovaleric anhydride, but this was undoubtedly due to the above-noted secondary process of decarboxylation of the intermediate product of this condensation.

Reaction of Silicoanhydrides of Carboxylic Acids with Furfural and Thiophene-2-aldehyde

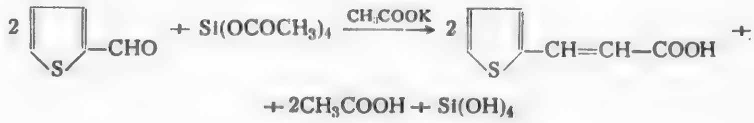
Reaction components (in g)					Reaction conditions		Reaction products								Melting points reported in the literature
Acid anhydride								Yield		Constants and analytical data					
											% C		% H		
Name	Quantity	furfural	potassium acetate	potassium carbonate	temperature	duration of heating (hrs)	Acid	in g	in % of theory	Melting point	found	calc.	found	calc.	
Silicoacetic anhydride	26.4	9.6	—	13.8	145—150°	5	β-(Furyl-2)-acrylic	3.6	26.0	140—141° *	—	—	—	—	140° [8]
	33.0	9.6	9.8	—	150—155	10		8.1	59.0	140—141 *	—	—	—	—	141 [9]
	26.4	9.6	9.8	—	150—155	5		7.3	53.0	140—141 *	—	—	—	—	
Silicopropionic	32.0	9.6	—	13.8	155—160	10	α-Methyl-β-(furyl-2)-acrylic	10.7	70.5	115.5—116.2	63.26, 63.29	63.15	5.43, 5.46	5.30	116 [10]
	32.0	9.6	—	13.8	155—160	5		6.2	41.0	115.6—116.2	—	—	—	—	
Silicobutyric	22.0	4.8	—	6.9	100	30	α-Ethyl-β-(furyl-2)-acrylic	5.0	60.0	98.5—99	65.14, 65.10	65.05	6.09, 6.04	6.06	95.5—97 [3]
	37.6	9.6	—	13.8	100	15		5.9	36.0	98.5—99	—	—	—	—	
	19.0	4.8	—	6.9	165—170	5		3.7	44.5	98.5—99	—	—	—	—	
Silicovaleric	11.0	2.4	—	3.5	145—150	8	α-Propyl-β-(furyl-2)-acrylic	1.5	33.0	100—101	66.53, 66.61	66.65	6.72, 6.69	6.71	Not described in the literature
Silicoisovaleric	43.0	9.6	—	13.8	120—125	15	α-Isopropyl-β-(furyl-2)-acrylic	0.6	3.3	114—114.5	66.50, 66.59	66.65	6.79, 6.79	6.71	114 [3]
Silicocaproic	49.0	9.6	—	13.8	155—160	10	α-Butyl-β-(furyl-2)-acrylic	5.1	26.0	73.8—74.2	68.05, 68.08	68.01	7.29, 7.31	7.26	Not described in the literature
		Thiophene-2-aldehyde													
Silicoacetic anhydride	17.0	5.6	4.9	—	150—155°	10	β-(Thienyl-2)-acrylic	1.9	25.0	144.5—145**	—	—	—	—	138 [7]
	18.0	3.36	5.1	—	170—175	10		3.7	80.0	144.5—145	—	—	—	—	144—145 [11]

* No depression observed in mixed melting test with authentic β-(furyl-2)acrylic acid.

** No depression observed in mixed melting test with authentic β-(thienyl-2)-acrylic acid; 3.25 g (58%) of unchanged thiophene-2-aldehyde with b.p. 196-198° was also isolated.

In the present work we also studied the condensation of thiophene-2-aldehyde with silicoacetic anhydride, which gave β-(thienyl-2)-acrylic acid. The latter was described by Biderman [7] who prepared it by condensation of thiophene-2-aldehyde with acetic anhydride in presence of potassium acetate at the boil, but did not state the yield.

We found that condensation of thiophene-2-aldehyde with silicoacetic anhydride in presence of potassium acetate calls for more drastic conditions than are needed in the corresponding condensation of furfural. Under the conditions most favorable for condensation of furfural, the yield of β-(thienyl-2)-acrylic acid was only 25%, and 58% of the aldehyde was recovered unchanged, whereas heating to 170-175° for 10 hours increased the acid yield to 80%.



EXPERIMENTAL

The previous procedure [1] was employed for preparation of silicoanhydrides of saturated monobasic acids, for their condensation with furfural and with thiophene-2-aldehyde (b.p. 80° at 12 mm, 198° at 756 mm, n_D^{20} 1.5889, d_4^{20} 1.224 [8]), as well as for isolation of the reaction products (see table for results obtained).

SUMMARY

The possibility of application of silicoanhydrides of saturated monobasic organic acids for synthesis of α, β unsaturated acids of the furan and thiophene series was demonstrated by preparations of β-(furyl-2)- and α-alkyl-β-(furyl-2)-acrylic acids, as well as of β-(thienyl-2)-acrylic acid, by condensation of furfural and thiophene-2-aldehyde with the appropriate silicoanhydrides.

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THE CHLORINATION OF n-HEXANE AND n-HEPTANE

V. A. Nekrasova

Processes of chlorination of alkanes have repeatedly attracted the attention of many investigators in the search for convenient routes for passage from the chemically inert paraffins to the reactive halogenated derivatives. The great interest in the field of photochemical chlorination of hydrocarbons is due mainly to the possibility of successful application of the process at low temperatures with a higher degree of conversion and with a high productivity per unit of reaction space. No less interesting is the catalytic chlorination of alkanes.

The literature is lacking in any data about chlorination of higher alkanes beyond the first five members of the series.

Lemke and Tishchenko [1] carried out the photochemical chlorination of n-pentane in the liquid phase and obtained 60% of dichlorides, 28-34% of monochlorides and 7-8% of trichlorides.

E. T. McBee and H. B. Hass [2] carried out the photochemical chlorination of n-butane, isobutane, n-pentane and isopentane.

A. V. Topchiev, B. A. Krentsel and L. N. Andreev [3] studied the photochemical chlorination of n-butane in a flow apparatus. Use has also been made [4] of series of heterogeneous catalysts for the chlorination of n-butane, an iron catalyst was found to be the most active. B. A. Krentsel and N. A. Pokotilo [5] chlorinated n-butane in presence of active carbon and Askanite* in the pure form or impregnated with copper chloride. A number of authors [6-11] chlorinated higher alkanes in presence of active carbon, silica gel and chlorides of some metals.

In the present work we studied the photochemical chlorination of n-heptane and the catalytic chlorination of n-hexane and n-heptane.

Photochemical chlorination of heptane was found to give dichloropentanes in high yield. The most active of the catalysts tested was cobalt chloride deposited on pumice. Its high activity is probably due to its ability to initiate chain growth (development of free radicals).

$$CoCl_2 \longrightarrow CoCl + Cl$$

$$CoCl + Cl + C_6H_{14} \longrightarrow HCoCl_2 + C_6H_{13}$$

$$HCoCl_2 \xrightarrow{\text{heating}} CoCl + HCl$$

$$CoCl + Cl_2 \longrightarrow CoCl_2 + Cl$$

$$Cl + C_6H_{13} \longrightarrow C_6H_{13}Cl$$

The intially formed hexyl chloride can react with elemental chlorine to form 1,6-dichlorohexane [12].

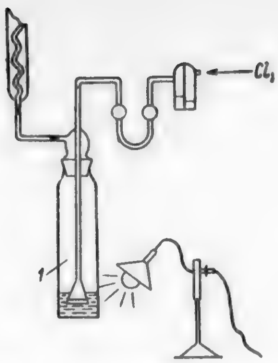
EXPERIMENTAL

Photochemical Chlorination

The initial n-heptane had b.p. 98.4° (754 mm), d_4^{20} 0.6843, n_D^{20} 1.3879.

Chlorination was performed in the apparatus illustrated in the diagram.

*As in original – Publisher's note.



Set-up for photochlorination of hydrocarbons.

Hydrocarbon in reactor 1 was irradiated with an electric lamp. Chlorine from a cylinder passed through a drying bottle (containing sulfuric acid) and a flowmeter and entered the reactor through a capillary tube or a porous glass filter. The light source was an electric lamp (200 watt) which during the first 15 minutes of the experiment was placed at a distance of 5 cm from the reactor and subsequently at a distance of 14 cm.

Experiments were run with various volumetric ratios of hydrocarbon to chlorine. The latter was admitted at a rate of 0.76 liter/hour. Results of the best experiments are shown in Table 1. The latter shows that increase in the amount of chlorine is accompanied by a fall in yield of dichlorides.

31.2 g of condensate from experiment 2 was washed and dried before being subjected to careful fractionation. The following fractions were obtained:

1st, b.p. 146-148° (754 mm), d_4^{20} 0.8672, n_D^{20} 1.4222; chlorine content found %: 26.4; calculated %: 26.34; 2nd, b.p. 159-161° (754 mm), d_4^{20} 0.8726, n_D^{20} 1.4284; chlorine content found %: 26.4; calculated %: 26.34; 3rd, b.p. 119-120° (28 mm), d_4^{20} 1.0980, n_D^{20} 1.4707; chlorine content found %: 42.50; calculated %: 42.47.

TABLE 1

Photochemical Chlorination of n-Heptane in the Liquid Phase with Dry Chlorine at 14-16°

Expt. No.	Chlorine taken (liters)	Molar ratio of n-heptane to chlorine	Yield of condensate (g)	Composition of condensate (%)			
				monochlorides		dichlorides	polychlorides
				secondary	1-chloroheptane		
1	10.9	1 : 1	28.6	12.3	11.5	76.2	—
2	21.8	1 : 2	31.2	10.2	9.7	80.0	—
3	27.3	1 : 2.2	31.5	4.3	4.5	74.9	16.3
4	32.7	1 : 3	31.9	—	—	61.6	36.4

Note. 21.6 g of n-heptane was consumed in each experiment in 4 hours.

On the basis of comparison with literature data [12], we see that the 1st fraction corresponds to 2-chloroheptane, the 2nd to 1-chloroheptane and the 3rd to 1,7-dichloroheptane.

In subsequent experiments the proportion of chlorine was increased by a factor of 3 and the reaction period to 6.5 hours. The reaction product consisted solely of polychlorides; mono- and dichlorides could not be detected.

Catalytic Chlorination of n-Hexane and n-Heptene

Characteristics of starting hydrocarbons. n-Hexane: b.p. 68.7° (754 mm), d_4^{20} 0.6594, n_D^{20} 1.3749 n-Heptane: b.p. 98.4° (754 mm), d_4^{20} 0.6837, n_D^{20} 1.3877.

Experiments were performed in a flow apparatus. The action of the following catalysts was investigated: active carbon, aluminum chloride on active alumina, ferric chloride on wood charcoal, asbestos and pumice, nickel chloride on pumice, copper chloride on pumice, magnesium chloride on pumice and on magnesia, barium chloride on magnesia, cobalt chloride on silica gel active alumina, potsherds and pumice. All of the catalysts (except aluminum chloride on alumina) contained 15% of metal chlorides, and they were tested for catalytic activity under standard conditions: temperature 320°, catalyst volume

100 ml, molar ratio of hydrocarbon to chlorine 1 : 2, space velocity for n-hexane 0.17 and for n-heptane 0.18, chlorine flow rate 0.55 liter/hour.

The first series of hexane chlorinations $C_6H_{14} + 2Cl_2 \rightarrow C_6H_{12}Cl_2 + 2HCl$ were carried out with the aim of selection of the best catalyst at 320°.

After they had been washed and dried, the catalyzates were fractionally distilled in a 40-plate column. The fractions were analyzed for chlorine content and their composition was determined on the basis of the analytical data and the physicochemical constants. As an example, we present the data for the condensate from experiment 19.

Fractions obtained: 1st, b.p. 122-124° (758 mm), d_4^{20} 0.8732, n_D^{20} 1.4136; chlorine found %: 29.58; calculated %: 29.4; 2nd, b.p. 134-136° (758 mm), d_4^{20} 0.8780, n_D^{20} 1.4232; chlorine found %: 29.53; calculated %: 29.4; 3rd, b.p. 93.0-94.5° (22 mm), d_4^{20} 1.086, n_D^{20} 1.4570; chlorine found %: 45.78; calculated %: 45.74.

TABLE 2

Catalytic Chlorination of n-Hexane in the Vapor Phase

Expt. No.	Catalysts	Yield of condensate (%)	Unreacted hydrocarbon (%)	Composition of condensate (in %) calculated on hydrocarbon reacted			
				sec. chlorides	1-chlorohexane	dichlorides	polychlorides
5	Active carbon	10.5	91.9	8.1	—	—	—
6	Aluminum chloride (3%) on active alumina	10.6	66.6	33.4	—	—	—
7	Ferric chloride on wood charcoal	12.5	90.0	5.2	3.8	—	—
8	Ferric chloride on asbestos	12.3	41.9	55.3	2.8	—	—
9	Ferric chloride on pumice	14.2	11.5	69.2	19.3	—	—
10	Nickel chloride on pumice	8.5	53.2	46.8	—	—	—
11	Cupric chloride on pumice	10.5	63.0	18.3	15.9	—	—
12	Magnesium chloride on pumice	12.9	65.8	62.5	21.6	—	—
13	Magnesium chloride on magnesia	12.7	63.0	37.0	—	—	—
14	Barium chloride on magnesia	12.8	72.4	27.6	—	—	—
15	Cobalt chloride on silica gel	10.9	22.2	75.3	2.5	—	—
16	Cobalt chloride on active alumina	11.0	83.5	16.5	—	—	—
17	Cobalt chloride on potsherds	14.9	83.0	51.6	8.5	23.0	12.0
18	Cobalt chloride on pumice	15.2	60.7	2.5	4.7	53.5	—
19	Pumice	14.9	9.8	56.0	5.5	18.7	9.0

Note. 10.8 g hexane and 5.45 g chlorine were taken in each experiment.

Comparison of the properties of the fractions with the literature data shows that the 1st fraction is a mixture of secondary chlorides, the properties of the 2nd fraction resemble those of 1-chloroheptane, and those of the 3rd fraction resemble those of 1,6-dichlorohexane.

Data obtained for various catalysts are included in Table 2 for comparison of their activities under standard conditions. It appears that cobalt chloride deposited on granular pumice is the best catalyst. This catalyst was in use for 170 hours without loss of activity.

Catalytic chlorination of n-heptane was likewise carried out at 330-340° in presence of $CoCl_2$ on pumice under standard conditions. The catalyzates were washed and dried before being fractionated in a vacuum-column The following fractions were obtained:

1st, b.p. 46° (19.5 mm), d_4^{20} 0.8670, n_D^{20} 1.4220; chlorine found %: 26.43; calculated %: 26.34; 2nd, b.p. 63° (27 mm), d_4^{20} 0.8726, n_D^{20} 1.4284; chlorine found %: 26.41; calculated %: 26.34; 3rd, b.p. 119-120° (28 mm), d_4^{20} 1.098, n_D^{20} 1.4707; chlorine found %: 42.5; calculated %: 42.47.

The 1st fraction corresponded to 2-chloroheptane, and the 2nd and 3rd were assumed to be 1-chloroheptane and 1,7-dichloroheptane, respectively. The yield of the 1,7-dichloroheptane fraction was 32% calculated on the reacted n-heptane. The determined constants are in agreement with the literature data [12].

SUMMARY

1. Photochemical chlorination of n-heptane in the liquid phase was studied and the conditions for preparation of dichloropentanes in good yields were established. The need for thorough dispersion of the chlorine during photochemical chlorination of alkanes was demonstrated.

2. The catalytic properties of chlorides of various metals in the chlorination of alkanes were studied.

3. Cobalt chloride deposited on pumice was found to be the most efficient of the catalysts examined.

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THE PROBLEM OF THE PRODUCTION OF ALIPHATIC ALCOHOLS FROM PETROLEUM HYDROCARBONS

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The problem of the production of C_6-C_{12} aliphatic alcohols from petroleum hydrocarbons via their chlorination products is not discussed at all in the literature, although the hydrolysis of the lower chloroalkanes has been studied fairly closely.

Studies have been made, for example, the hydrolysis of isoamyl chloride at 170-180° which gives a 28% yield of isoamyl alcohol [1, 2]. Confirmation of these results was later obtained [3].

Liquid-phase hydrolysis of butyl chloride with milk of lime in an autoclave gave an 80% yield of primary n-butyl alcohol [4, 5].

With the objective of hydrolyzing C_6-C_{12} chloroalkanes we made use of chlorides synthesized from n-alkanes isolated from gasoline by straight-running of Crimean oil, the paraffinic portion of which consists almost exclusively of alkanes of normal structure. Other Black Sea oils (Il'sk and Khadyzhensk) have approximately the same composition.

EXPERIMENTAL

Hydrocarbons of normal structure were separated from isomers and cyclic hydrocarbons by formation of urea complexes [6]. They were then subjected to fine rectification in a 70-plate column. The properties of the isolated hydrocarbons are presented in Table 1.

TABLE 1

Properties of n-Alkanes Isolated from Gasoline from Crimean Oil

Hydrocarbons	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}
n-Hexane	68— 69° (751)	0.6594	1.3750
n-Heptane	98— 99 (754)	0.6838	1.3878
n-Octane	125—126 (754)	0.7026	1.3975
n-Nonane	150—151 (751)	0.7177	1.4054
n-Decane	174—175 (750)	0.7298	1.4120
n-Undecane	195—196 (757)	0.7403	1.4172
n-Dodecane	215.5—217 (755)	0.7489	1.4218

We performed the vapor-phase thermal chlorination of n-alkanes in presence of nitrogen dioxide [7].

The prepared chlorides were washed with water, sodium carbonate solution, and again with water, dried with anhydrous calcium chloride, and subjected to fine rectification in a 40-plate, glass-packed column. The chlorine content of the chloroalkanes was determined by double combustion [8].

The properties of the monochloro derivatives are presented in Table 2.

The primary C_6-C_{12} monochlorides were hydrolyzed in a stainless steel, rotating autoclave. Optimum conditions of hydrolysis were estabished in preliminary experiments and were employed in the subsequent hydrolysis of the other chloroalkanes.

TABLE 2

Physicochemical Properties of the Isolated Primary Monochlorides

Chloroalkanes	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D		Chlorine content (%)	
				found	calc.	found	calc.
1-Chlorohexane	135—137° (758)	0.8760	1.4236	35.0	35.04	29.53	29.19
1-Chloroheptane	159—161 (756)	0.8726	1.4284	39.36	39.40	26.62	26.37
1-Chlorooctane	183—185 (757)	0.8709	1.4311	44.15	44.01	23.98	23.88
1-Chlorononane	202—204 (755)	0.8702	1.4360	48.61	48.63	21.96	21.82
1-Chlorodecane	222—224 (754)	0.8697	1.4380	53.29	53.25	20.34	20.09
1-Chloroundecane	240—242 (754)	0.8692	1.4399	57.83	57.86	18.85	18.59
1-Chlorododecane	255—257 (758)	0.8686	1.4418	62.39	62.48	17.79	17.25

As an example we give the results of hydrolysis of 1-chloroheptane: 100 g 1-chloroheptane was charged into the 1-liter autoclave followed by 233 ml 20% sodium hydroxide solution and 50 g emulsifying agent (product of sulfochlorination of heavy fractions of Synthine). The autoclave was thereupon heated to 170-175° while being rotated at a constant speed of 150 revs. per min. During this operation the pressure in the autoclave rose to 20-25 atm. At the termination of the experiment, the upper layer was separated from the reaction mass and acidified with 20% sulfuric acid. The resulting alcohol was distilled off in steam together with unreacted haloalkane and unsaturated hydrocarbon.

The isolated crude product was washed with sodium carbonate solution and water, thoroughly dried with calcined potassium carbonate, and subjected to fine fractionation. Yield of heptyl alcohol 61.26 g (80%), b.p. 176-177° (755 mm), d_4^{20} 0.8218, n_D^{20} 1.4241.

The properties of the other prepared alcohols are presented in Table 3.

TABLE 3

Physicochemical Properties of the Isolated Primary Aliphatic Alcohols

Alcohols	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	MR_D	
				found	calculated
n-Hexyl	155—156° (754)	0.8185	1.4179	31.45	31.43
n-Heptyl	176—177 (755)	0.8218	1.4241	36.09	36.05
n-Octyl	195—196 (754)	0.8245	1.4292	40.74	40.67
n-Nonyl	215—216 (753)	0.8273	1.4334	45.35	45.29
n-Decyl	229—230 (754)	0.8291	1.4368	49.99	49.91
n-Undecyl	146—147 (25)	0.8354	1.4404	54.40	54.52
n-Dodecyl	149—150 (20)	0.8372	1.4439	59.11	59.14

SUMMARY

1. The possibility of synthesis of primary aliphatic alcohols fron the corresponding alkanes via their chlorination products was studied.

2. Optimum conditions were established for hydrolysis of the primary chloroalkanes in 75-80% yield.

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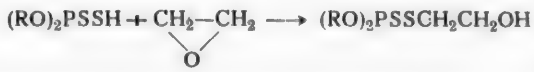
REACTION OF DIALKYL DITHIOPHOSPHATES WITH ETHYLENE SULFIDE

T. A. Mastriukova, V. N. Odnoralova and M. I. Kabachnik

Some time ago we published an article about the addition of dialkyl dithiophosphates to ethylene oxide [1]. As shown in that paper, these substances react smoothly with formation of β-hydroxy-substituted esters dithiophosphoric acid.



The present study is devoted to the examination of the reaction of dialkyl dithiophosphates with ethylene sulfide.

As is known [2-4], ethylene sulfide is a rather reactive compound which resembles ethylene oxide in many reactions. Thus, mercaptans, phenols, and amines add to ethylene sulfide with opening of its three-membered ring [3-6]. Under the action of aqueous solutions of bases – alkali, pyridine, diethylamine – there takes place a rapid polymerization of ethylene sulfide [2, 4, 8]. As to acids, those like sulfuric and acetic cause polymerization of the ethylene sulfide [2, 7]; hydrogen chloride and hydrogen sulfide, on the other hand, add to ethylene sulfide [2, 3]. Addition of hydrogen chloride also takes place under the action of concentrated hydrochloric acid [2].

Dialkyl dithiophosphates are strong acids with ionization constants of the order of 10^{-2} in water [9]. Therefore one might presuppose that they would cause the polymerization of ethylene sulfide. On the other hand one might expect their addition with opening of the three-membered ring, analogous to that of addition of hydrogen sulfide and hydrogen chloride. In the latter case the reaction would proceed analogously to the addition of dialkyl dithiophosphates to ethylene oxide.

The study showed that dialkyl dithiophosphates add to ethylene sulfide with formation of dialkyl S-β-mercaptoethyl dithiophosphates.

In contrast to ethylene oxide this addition occurs under more drastic conditions: thus while ethylene oxide reacts at room temperature, ethylene sulfide forms the addition product only after being heated.

In Table 1 are given the constants and the analyses of the dialkyl S-β-mercaptoethyl dithiophosphates prepared by us. These are colorless liquids which are unstable thermally. They are readily soluble in organic solvents but are insoluble in water. They are decomposed by alkalies analogously to dialkyl β-hydroxyethyl dithiophosphates.

The sulfhydryl group of β-mercaptoethyl dithiophosphates is readily acetylated. Thus, from dialkyl S-β-mercaptoethyl dithiophosphates there were prepared the corresponding acetyl derivatives by the reaction with acetic anhydride in the presence of pyridine:

TABLE 1

Dialkyl S-β-Mercaptoethyl Dithiophosphates and Their Derivatives.

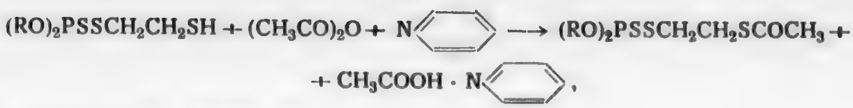
Ordinal No.	Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Yield (%)	Analyses (in %) C found	C calc.	H found	H calc.	P found	P calc.	S found	S calc.
1	$(CH_3O)_2PSSCH_2CH_2SH$	105–106° (1)	1.5690	1.2882	60	22.17, 22.06	22.01	5.04, 5.03	5.08	13.76, 13.90	14.19	43.82, 43.92	44.07
2	$(C_2H_5O)_2PSSCH_2CH_2SH$	110–112 (1.5)	1.5438	1.1966	64	29.59, 29.47	29.25	6.17, 6.11	6.13	12.40, 12.40	12.57	39.00, 38.76	39.04
3	$(C_3H_7O)_2PSSCH_2CH_2SH$	113–115 (1)	1.5312	1.1424	46	35.61, 35.50	35.01	6.99, 6.99	6.98	10.92, 10.80	11.29	34.83, 34.61	35.05
4	$(iso\text{-}C_3H_7O)_2PSSCH_2CH_2SH$	110–112 (1.5)	1.5230	1.1287	44	35.49, 35.56	35.01	7.01, 7.02	6.98	11.16, 11.36	11.29	35.00, 35.00	35.05
5	$(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SH$	129–131 (1.5)	1.5198	1.0966	46	—	—	—	—	10.16, 10.40	10.24	31.94, 31.79	31.81
6	$(C_2H_5O)_2PSSCH_2CH_2SCOCH_3$	135–137 (2.5)	1.5351	1.1994	22	33.56, 33.49	33.32	6.11, 6.02	5.94	10.55, 10.58	10.74	—	—
7	$(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SCOCH_3$	143–144 (2.5)	1.5170	1.1074	19	41.89, 42.09	41.83	7.38, 7.38	7.31	8.76, 8.85	8.82	28.29, 28.16	27.92
8	$(C_2H_5O)_2PSSCH_2CH_2SCH_3$ *	111–113 (1)	1.5388	1.1708	51	32.56, 32.64	32.28	6.61, 6.60	6.58	—	—	36.43, 36.73	36.94
9	$(C_3H_7O)_2PSSCH_2CH_2SCH_3$	128–129 (1.5)	1.5270	1.1229	62	37.80, 38.01	37.47	7.36, 7.28	7.30	10.52, 10.71	10.74	33.18, 33.01	33.35
10	$(iso\text{-}C_3H_7O)_2PSSCH_2CH_2SCH_3$	115 (1.5)	1.5179	1.1087	62	37.20, 37.20	37.47	7.39, 7.36	7.34	10.50, 10.44	10.74	33.20, 33.04	33.35

* Constants of substance No. 8 prepared previously [10]: b.p. 155-156° at 3 mm, n_D^{20} 1.5405, d_4^{20} 1.1699.

TABLE 2

Reactions of Ethylene Sulfide with Dialkyl Dithiophosphates

Ordinal No.	Formula of reaction product	Am'ts of starting materials in moles: acid	ethylene sulfide	Reaction conditions: temperature	time in hours	n_D^{20}	d_4^{20}	Analyses in % C found	C calc.	H found	H calc.	P found	P calc.	S found	S calc
1	$(CH_3O)_2PSSCH_2CH_2SH$	0.06	0.07	72–74°	9.5	1.5738	1.2915	21.98, 21.80	22.01	4.84, 4.90	5.08	13.86, 14.15	14.19	43.77, 44.11	44.07
2	$(C_2H_5O)_2PSSCH_2CH_2SH$	0.07	0.08	72–74	9.5	1.5485	1.2041	29.17, 29.39	29.25	6.04, 6.03	6.13	12.58, 12.57	12.57	39.11, 39.13	39.04
3	$(C_3H_7O)_2PSSCH_2CH_2SH$	0.06	0.07	76–78	12	1.5370	1.1522	35.22, 35.29	35.01	6.92, 6.83	6.98	—	—	35.53, 35.44	35.05
4	$(iso\text{-}C_3H_7O)_2PSSCH_2CH_2SH$	0.05	0.07	77–78	13	1.5365	1.1506	35.06, 35.06	35.01	6.88, 6.92	6.98	11.20, 11.05	11.29	34.48, 34.62	35.05
5	$(iso\text{-}C_4H_9O)_2PSSCH_2CH_2SH$	0.045	0.06	75–80	14	1.5265	1.1088	39.87, 39.72	39.71	7.59, 7.47	7.59	10.07, 10.13	10.24	32.35, 32.34	31.81



the constants and the analyses of these products are shown in Table 1.

β-Mercaptoethyl dithiophosphates react with diazomethane in the presence of methyl alcohol; the sulfhydryl group is methylated thereby:

$$(RO)_2PSSCH_2CH_2SH + CH_2N_2 \longrightarrow (RO)_2PSSCH_2CH_2SCH_3 + N_2$$

Substances of this type have been known earlier [10]; they are effective systemic insecticides. Triethyl dithiophosphate was isolated as the main product in an attempt to conduct an alkylation of diethyl S-β-mercaptoethyl dithiophosphate with ethyl bromide in the presence of sodium carbonate. A polymer of ethylene sulfide formed along with the triethyl dithiophosphate when sodium hydroxide was employed in this reaction. Evidently the reaction may be represented by the following scheme:

$$n + 2(C_2H_5O)_2PSSCH_2CH_2SH + nC_2H_5Br + nNaOH \longrightarrow n(C_2H_5O)_2PS(SC_2H_5) +$$
$$+ H_2S + nNaBr + nH_2O + (C_2H_5O)_2PSS(CH_2CH_2S)_{n+2}PS(OC_2H_5)_2$$

Similar reactions are known among esters of thiocarboxylic acids which contain a sulfhydryl group in the β-position [11].

EXPERIMENTAL

The dialkyl dithiophosphates necessary for the reaction were prepared and purified according to the previously known methods [12]. We used for the reactions ethylene sulfide [4] which was stabilized with ethylmercaptan [13].

Preparation of Dialkyl S-β-Mercaptoethyl Dithiophosphates

The mixture of the dialkyl dithiophosphate and ethylene sulfide was placed into a steel bomb with a glass liner. The sulfide was taken usually in slight excess. Then the bomb was heated to 70-80° for 9.5 to 14 hours, depending on the size of the radical of the dialkyl dithiophosphate used. The end of the reaction was determined by the absence of the acid test to Congo red in the reaction mixture. The excess ethylene sulfide was removed in vacuum and the residual almost colorless product was analyzed and its constants were determined. Then the crude product was distilled in vacuum in nitrogen atmosphere. In all cases the undistilled product was close to the distilled product in physical constants. In Table 2 are shown the data on the reaction of ethylene sulfide with dialkyl dithiophosphates, as well as the constants of the undistilled substances and their analyses; in Table 1 are shown the constants and analyses of the distilled substances.

Acetylation of Dialkyl S-β-Mercaptoethyl Dithiophosphates

To a solution of dialkyl S-β-mercaptoethyl dithiophosphate in dry pyridine, acetic anhydride was added dropwise. The reaction proceeded with slight heat effect. After several hours the reaction mixture was decomposed with 5% acetic acid with cooling. The organic layer was separated, and the aqueous layer was extracted with ether. The combined extracts were washed with sodium carbonate and water. After drying over calcined sodium sulfate, the reaction mixture was fractionated.

Diethyl S-β-acetylmercaptoethyl dithiophosphate was prepared from 7.8 g (0.03 mole) of diethyl S-β-mercaptoethyl dithiophosphate and 4.3 g (0.04 mole) of acetic anhydride in 10 ml of pyridine; the constants and analyses are shown in Table 1.

Diisobutyl S-β-acetylmercaptoethyl dithiophosphate was prepared from 6.4 g (0.02 mole) of diisobutyl S-β-mercaptoethyl dithiophosphate and 3.4 g (0.03 mole) of acetic anhydride in 10 ml. of pyridine (see Table 1).

Alkylation of Dialkyl S-β-Mercaptoethyl Dithiophosphates with Diazomethane

To the solution of 0.02 mole of dialkyl S-β-mercaptoethyl dithiophosphate in ether in the presence of 5 ml of methyl alcohol, there was added dropwise an ethereal solution of diazomethane, taken in excess. The formation of nitrogen was completed within 20-30 minutes. On the following day the excess diazomethane was removed, the ethereal solution was washed with sodium carbonate and water and was dried over sodium sulfate. After distillation of the ether, the reaction product was distilled in vacuum. The constants and analyses of the products are shown in Table 1.

Alkylation of Diethyl S-β-Mercaptoethyl Dithiophosphate in the Presence of Sodium Carbonate

The mixture of 16.2 g (0.066 mole) of diethyl S-β-mercaptoethyl dithiophosphate, 9 g (0.082 mole) of ethyl bromide and 4.2 g (0.04 mole) of finely powdered sodium carbonate in 50 ml of dry acetone was refluxed for 8.5 hours. After that, the precipitate was filtered off and was washed; 6.4 g of the precipitate was isolated. Acetone was distilled from the filtrate, the residue was washed with sodium carbonate and water and was then extracted with ether. After being dried over calcined sodium sulfate and after a vacuum distillation, there was obtained 4 g of triethyl dithiophosphate (33% calculated on the reacted diethyl S-β-mercaptoethyl dithiophosphate). The product had the following constants:

B.p. 104-105° at 7 mm, n_D^{20} 1.5030, d_4^{20} 1.1146. *

Found %: C 34.02, 33.96; H 7.23, 6.98. $C_6H_{15}O_2PS_2$. Calculated %: C 33.64; H 7.01.

A higher boiling fraction was also isolated during the distillation; this represented the unreacted diethyl S-β-mercaptoethyl dithiophosphate: b.p. 106-109° at 1.5 mm, n_D^{20} 1.5411, d_4^{20} 1.1903.

When the reaction was conducted under these conditions but in the presence of sodium hydroxide, a polymer of ethylene sulfide was isolated from the precipitate which contained sodium bromide This polymer contained phosphorus and sulfur and was insoluble in organic solvents (alcohol, acetone, ether).

According to its analysis the polymer approximated $(C_2H_5O)_2PSS(CH_2CH_2S)_nPS(OC_2H_5)_2$, where n might be from 18 to 20.

Found %: C 38.39, 39.26; H 6.86, 6.83; P 4.36, 4.36; S 45.36, 45.36.

SUMMARY

1. The reaction of dialkyl dithiophosphates with ethylene sulfide was studied. It was shown that in this reaction there takes place the addition of dialkyl dithiophosphates to ethylene sulfide with formation of dialkyl S-β-mercaptoethyl dithiophosphates.

2. The presence of β-mercaptogroups in these compounds was proved by their acetylation and alkylation with diazomethane.

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* Constants of triethyl dithiophosphate prepared previously [14]: b. p. 115-115.5° at 10 mm, n_D^{20} 1.5013, n_4^{20} 1.1168.

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ORGANOPHOSPHORUS INSECTICIDES. SOME DERIVATIVES OF METHYLTHIOPHOSPHONIC AND METHYLDITHIO-PHOSPHONIC ACIDS

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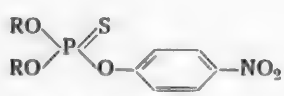
N. M. Gamper and L. F. Efimova

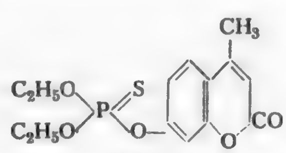
The majority of organophosphorus insecticides are derivatives of thiophosphoric, dithiophosphoric and pyrophosphoric acids [1-3]. In the literature a few insecticides are described which are derivatives of phosphonic and dithiophosphonic acids; among them are esters of methylphosphonic and methylthiophosphonic acids, containing substituted aryl [4], ethylxanthoyl [5] and other [4] groups, as well as the O-ethyl-O-p-nitrophenyl ester of phenylthionophosphonic acid (EPN) [6], which is the only insecticide of the series of thiophosphonic acids which has found a practical application.

In connection with this, it appeared interesting to synthesize a series of derivatives of alkylthio- and alkyldithiophosphonic acids, containing ester groups analogous to those possessed by the known insecticides of the series of thiophosphoric and dithiophosphoric acids and to evaluate their insecticidal action.

We prepared, as the simplest representatives, some derivatives of methylthiophosphonic and methyldithiophosphonic acids which contain atomic groupings analogous to those in Metafos (methyl parathion) (I), Tiofos (parathion) (II), Potasan (III), Karbofos (Malathion) (IV), Metasystox (V) and Merkaptofos (Systox) (VI).



(I) $R = CH_3$,
(II) $R = C_2H_5$.



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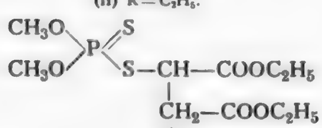

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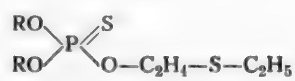


(V) $R = CH_3$,
(VI) $R = C_2H_5$.

The dichloride of methylthiophosphonic acid, which was prepared by the scheme below, was used as the starting material for the synthesis of these substances. The dichloride of methylphosphonic acid was synthesized by the method of Kinner and Perren [7]:

$$CH_3Cl + PCl_3 + AlCl_3 \longrightarrow CH_3PCl_3 \cdot AlCl_4,$$

$$CH_3PCl_3 \cdot AlCl_4 \xrightarrow{H_2O} CH_3POCl_2;$$

then, the oxygen of the phosphoryl group was replaced by sulfur by means of the method developed by us earlier [8]: $5CH_3P(O)Cl_2 + P_2S_5 = P_2O_5 + 5CH_3P(S)Cl_2$. By the reaction of the dichloride of methylthiophosphonic

acid with methyl, ethyl and n-propyl alcohols in the presence of triethyl amine there were synthesized the corresponding chlorides of acid esters of methylthionophosphonic acid (Table 1).

TABLE 1

Formula	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	MR_D found	MR_D calc.	Yield (%)	C (%) found	C (%) calc.	H (%) found	H (%) calc.
$(CH_3)(CH_3O)P(=S)Cl$	54—55° (21)	1.5085	1.2574	34.02	33.38	70	16.4, 16.5	16.6	3.9, 4.0	4.2
$(CH_3)(C_2H_5O)P(=S)Cl$	55—55.5 (8)	1.4952	1.1992	38.17	38.00	81	22.5, 22.5	22.7	4.8, 4.9	5.1
$(CH_3)(n\text{-}C_3H_7O)P(=S)Cl$	66—67 (7)	1.4890	1.1549	43.13	42.62	80	28.1, 27.9	27.8	6.0, 6.0	5.9

$$CH_3-\overset{S}{\overset{\|}{P}}(Cl)-Cl + ROH + (C_2H_5)_3N \longrightarrow CH_3-\overset{S}{\overset{\|}{P}}(OR)-Cl + (C_2H_5)_3N\cdot HCl,$$

where $R = CH_3$, C_2H_5 and $n\text{-}C_3H_7$.

The O-methyl-O-p-nitrophenyl ester of methylthionophosphonic acid (the laboratory number Gd-18) was prepared from the chloride of monomethyl ester of methylthionophosphonic acid and sodium p-nitrophenoxide, while from the acid ethyl ester of methylthionophosphonic acid and sodium p-nitrophenoxide and sodium salt of 4-methyl-7-hydroxycoumarin there were prepared correspondingly the O-ethyl-O-p-nitrophenyl (Gd-5) and O-ethyl-O-7-umbelliferonyl (Gd-19) esters of methylthionophosphonic acid.

The corresponding analogs of Malathion (Gd-27 and Gd-28) were synthesized by the reaction of the indicated acid chlorides with dimethyl and diethyl esters of α-mercaptosuccinic acid in the presence of triethylamine.

The chlorides of acid methyl and ethyl esters of methylthionophosphonic acid were also used for the synthesis of substances close in structure to Systox and Metasystox.

O-Methyl-O-β-methylmercaptoethyl (Gd-39) and O-ethyl-O-β-ethylmercaptoethyl (Gd-6) esters of methylthionophosphonic acid were prepared by the reaction ofchlorides of the above cited acids with β-hydroxydiethyl sulfide and β-hydroxyethyl methyl sulfide, respectively, in the presence of powdered sodium hydroxide.

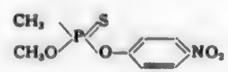
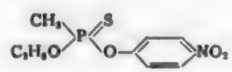
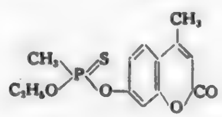
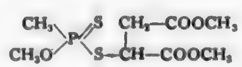
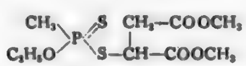
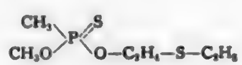
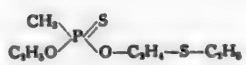
The yields, formulas, constants and analytical data of the synthesized substances are shown in Table 2

EXPERIMENTAL

Chlorides of acid esters of methylthiophosphonic acid. To 0.1 mole of dichloride of methylthiophosphonic acid [8] in 100 ml of absolute ether there was added, slowly and with cooling by means of water, a mixture of 0.1 mole of anhydrous alcohol and 0.1 mole of triethylamine. Then the reaction mixture was heated on a water bath for 30-40 minutes, after which the precipitated triethylamine hydrochloride was separated and the filtrate distilled in vacuum after the removal of ether. The constants, yields and analytical data for the compound thus prepared are shown in Table 1.

O-Alky -O-p-nitrophophenyl esters of methylthionophosphonic acid (Gd-5 and Gd-18; Table 2). To sodium ethoxide prepared from 0.1 g-atom of sodium and 100 ml of anhydrous alcohol, there was added in small portions a solution of 0.1 mole of p-nitrophenol in 100 ml of dry alcohol, after which the chloride of acid alkyl ester of methylthionophosphonic acid (0.1 mole) was added slowly. The precipitate of sodium chloride was separated, the filtrate was evaporated in vacuum, and the residue crystallized, after chilling with dry ice; it was then recrystallized from petroleum ether.

TABLE 2

Lab. No.	Formula	Boiling or melting point	n_D^{20}	d_4^{20}	MR_D		Yield (in %)	C(%)		H(%)		P(%)		S(%)	
					found	calc.		found	calc.	found	calc.	found	calc.	found	calc.
Gd-18		m.p. 52—53°	—	—	—	—	71	38.6, 38.8	38.9	4.1, 4.0	4.1	12.4, 12.3	12.5	12.8, 12.7	12.9
Gd-5		m.p. 35—36	—	—	—	—	84	41.3, 41.5	41.3	4.7, 4.7	4.6	11.6, 11.8	11.9	12.2, 12.2	12.3
Gd-19		m.p. 72—73	—	—	—	—	90	52.2, 52.2	52.3	5.0, 5.1	5.1	10.2, 10.4	10.4	10.5, 10.5	10.7
Gd-28		155—156 (3.5 мм)	1.5269	1.2765	68.84	68.19	38	33.7, 33.7	33.6	5.3, 5.2	5.3	10.7, 10.9	10.6	22.2, 22.3	22.4
Gd-27		166—167 (2 мм)	1.5065	1.1818	82.64	82.04	41	40.3, 40.3	40.2	6.4, 6.4	6.3	9.4, 9.3	9.3	19.8, 19.6	19.5
Gd-39		—	1.5204	1.1861	51.36	51.65	59	30.2, 30.1	30.0	6.5, 6.5	6.5	14.9, 15.0	15.3	32.3, 32.3	32.0
Gd-6		78 (1 мм)	1.5050	1.1124	60.84	60.79	52	36.6, 36.7	36.8	7.5, 7.7	7.6	13.9, 14.0	13.7	—	—

O-Ethyl-O-7-umbelliferonyl ester of methylthiophosphonic acid (Gd-19, Table 2). To sodium ethoxide prepared from 0.1 g-atom of sodium and 100 ml of anhydrous alcohol there was added 0.1 mole of 4-methyl-7-hydroxycoumarin, after which 0.1 mole of the chloride of acid ethyl ester of methylthionophosphonic acid was added slowly. Then, the mixture was heated on a steam bath until it attained neutral reaction to litmus The precipitate of sodium chloride was separated and alcohol was distilled in vacuum; the residue crystallized on chilling with dry ice and was twice recrystallized from petroleum ether.

O-Alkyl-S-1,2-dicarbalkoxyethyl esters of methyldithiophosphonic acid (Gd-27 and Gd-28, Table 2). To a mixture of 0.1 mole of the chloride of acid ester of methylthionophosphonic acid and 0.1 mole of triethylamine in 50 ml of absolute ether there was slowly added 0.1 mole of the ester of α-mercaptosuccinic acid, after which the mixture was heated on a water bath for one hour. The precipitated triethylamine hydrochloride was separated, the filtrate was washed with water and dried over sodium sulfate. After the removal of ether, the residue was distilled in vacuum.

O-Akyl-O-β-alkylmercaptoethyl esters of methylthionophosphonic acid (Gd-6 and Gd-39; Table 2). β-Hydroxyethyl alkyl sulfide (0.1 mole) and 0.1 mole of sodium hydroxide were placed in 50 ml of anhydrous benzene. Then, 0.1 mole of the chloride of the acid ester of methylthionophosphonic acid was added slowly. The mixture was heated on a water bath of 60-70° for one hour, after which the precipitate of sodium chloride was separated and benzene was distilled in vacuum, after which the residue was distilled in vacuum (Gd-6) or freed of volatile admixtures by heating to 60° at 2 mm for two hours (Gd-39).

TABLE 3

Compound	95-100% kill of insects by emulsion of concentration shown (%)		Kill of Eurygaster insects (%) on seventh day after infestation /intraplant action of the emulsion
	Pseudococcus maritimus Ehrh.	Eurgygaster integriceps Put.	
Gd-18	0.015	0.005	—
Metafos	—	0.01	—
Gd-5	0.075	0.005	2.5
Tiofos	> 0.025	0.005	—
Gd-19	0.10	0.05	—
Potasan	0.015	—	—
Gd-28	0.025	> 0.05	5.0
Gd-27	0.15	> 0.05	0
Karbofos-1 (Malathion)	—	> 0.01	—
Gd-39	0.10	> 0.05	2.5
Gd-6	> 0.075	0.05	—

The synthesized compounds were evaluated in laboratory experiments as to insecticidal action of contact and intraplant activity.

Insecticidal properties by contact action were studied on insects of Eurygaster integriceps Put. by the method of immersion into the emulsion with exposure for five seconds and on larvae of advanced age of Pseudococcus maritimus Ehrh. by the method of direct spraying. The toxicity of the compounds was determined on the seventh day according to the concentration of the active principles of the emulsions which caused 95-100% kill of the of the Eurygaster insects and 95-100% dead or paralyzed specimens of the Pseudococcus larvae

The intraplant action of the compounds was examined on the insects of Eurygaster by the technique of preseeding seed treatment of grains of summer wheat. Wheat grains were moistened by 0.6% emulsion of the compounds and were dried in air, being then planted in pots one day later. The Eurygaster insects were deposited onto three-day old sprouts of wheat. The results of the experiment were determined by the mortality of the insects on the seventh day after deposition. As standard substances we used Metafos (I), Tiofos (II), Potasan (III), and Karbofos (Malathion) (IV). The data from the laboratory experiments are in Table 3.

In addition, some of the compounds, specifically Gd-27, Gd-28 and Gd-39 were tested as acaricides with intraplant activity in greenhouse experiments by the spraying technique with Tefranychus sp. on decorative plants; however,the compounds proved to be ineffective.

Among the derivatives of methylthiophosphonic acid only one compound Gd-18 (analog of Metafos) was more toxic in contact action than the corresponding derivative of thiophosphoric acid – Metafos. The other compounds, including Gd-6 (Systox analog), Gd-5 (Tiofos analog) and Gd-19 (Potasan analog) did not show advantages in insecticidal action in comparison with derivatives of thiophosphoric acid.

Substances Gd-27 and Gd-28, which are analogs of Malathion (Karbofos) were characterized by weaker contact insecticidal toxicity against the insects of Eurygaster than Malathion. Against Pseudococcus larvae

the substance Gd-27 was a weakly toxic substance, while Gd-28 was equivalent to Tiofos. Both these compounds lacked any intraplant activity.

Thus, the replacement of the alkoxy group in known insecticides from the series of thiophosphoric and dithiophosphoric acids by a methyl group leads to derivatives of methylthiophosphonic and methyldithiophosphonic acids which do possess insecticidal activity. However, only a few of them exceed in insecticidal action the corresponding derivatives of thiophosphoric and dithiophosphoric acids.

SUMMARY

1. Chlorides of acid esters of methylthionophosphonic acid, containing methoxy, ethoxy and propoxy groups, were prepared from the dichloride of methylthiophosphonic acid.

2. A series of derivatives of methylthiophosphonic and methyldithiophosphonic acids with groupings analogous to those in Tiofos, Metafos, Karbofos, Potasan and Systox were synthesized.

3. The insecticidal properties (contact and intraplant) of the synthesized compounds were studied in laboratory conditions on fall insects of Eurygaster integriceps Put. and on older larvae of Pseudococcus maritimus Ehrh. It was shown that the majority of the prepared compounds are insecticides, which are weaker in activity than are the known insecticides from the series of thiophosphoric and dithiophosphoric acids. Substance Gd-18 (analog of Metafos) exceeds in contact activity the action of Metafos as tested on the insects of Eurygaster integriceps.

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AN INVESTIGATION IN THE FIELD OF ALKANESULFONIC ACIDS

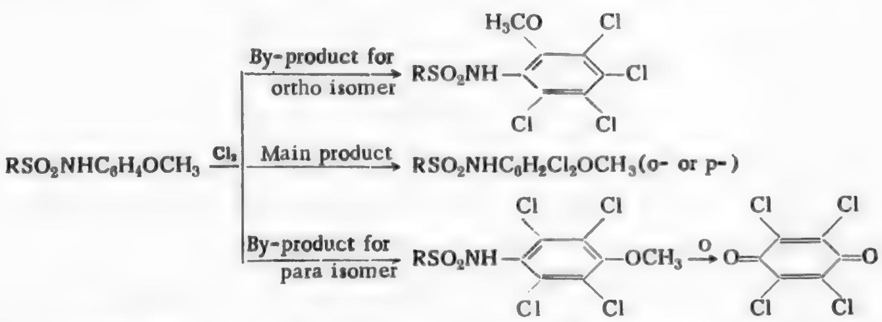
XVI. CHLORINATION OF ANISIDIDES OF ALKANESULFONIC ACIDS

A. G. Kostsova

We have shown in the previous paper [1] that in the chlorination of anilides of ethane- and butanesulfonic acids there are formed 2,4-dichloro anilides, while in the presence of zinc oxide this reaction leads to still greater yields of these chloro derivatives. The present work had for its purpose the study of the chlorination of o- and p-anisidides of the same sulfonic acids. As a result of the experiments run by us it was shown that the presence of a methoxyl group, as well as its position in the ring, have a notable effect on the character and the yields of the products formed. In addition, the radical of the sulfonic acid (ethyl or butyl) in turn influences (but to a lesser degree) the course of the reaction. Temperature and duration of chlorination have a lesser significance. In chlorination of ethane- and butanesulfoanisidides in the presence of zinc oxide the yields of the resulting compounds are considerably lowered in contrast to the similar chlorination of the unsubstituted anilides.

In chlorination of o-anisidides, dichloroanisidides are formed as the main reaction products, while in the case of derivatives of butanesulfonic acid the yields are lower under otherwise the same conditions. Besides the dichloroanisidides there were isolated in insignificant amounts some tetrachloroanisidides. The reaction products are colorless crystalline substances; the dichloroanisidides are relatively readily soluble in alcohol, while the tetrachloroanisidides are difficultly soluble. This property was used by us for their separation.

In chlorination of p-anisidides it was demonstrated that in the case of ethanesulfoanisidide, dichloro-p-anisidide is formed as the main product, but this occurs with lower yield than for dichloro-o-anisidide; an insignificant amount of tetrachlorobenzoquinone is also formed [2]. In case of butanesulfo-p-anisidide the dichloro derivative was not isolated but the tetrachlorobenzoquinone was isolated in a greater yield than in chlorination of the ethanesulfo-p-anisidide. It seems to us that the formation of this product is the result of a secondary process: evidently at first there is formed the tetrachloroanisidide (as it occurs in chlorination of the o-anisidides), which is then oxidized to tetrachlorobenzoquinone on contact with atmospheric oxygen. The reaction of chlorination of o- and p-anisidides may be expressed by the following general scheme:

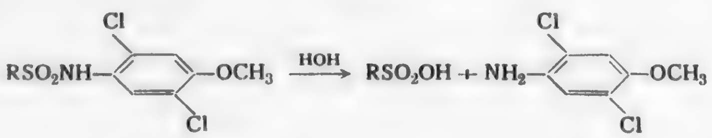


$R = C_2H_5,\ C_4H_9$

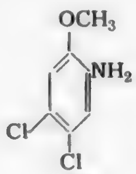
The results described above were obtained in chlorination of the substances with gaseous chlorine which was passed into the reaction mixture at the rate of 3-3.5 ml per second for various time intervals.

We also conducted the chlorination by another method — by mixing solutions of the anisidide and chlorine in in carbon tetrachloride, with the reactants being taken in this case in strictly equimolar amounts. It was shown that in this method of chlorination the same products are formed as in chlorination with gaseous unmetered chlorine, but the yields are lower. Monochloro and trichloro derivatives do not form in either case.

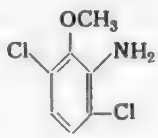
The position of chlorine in the aromatic nucleus of dichloroanisidides was proved by us by the reaction of hydrolysis; in case of dichloro-p-anisidide there was isolated 2,5-dichloroanisidine with m.p. 78-80° (according to literature data, m.p. 79-80°) [3]:



The position of chlorine in dichloro-o-anisidide is not completely clear since the dichloro-o-anisidine, with m.p. 90-92°, which was isolated by us after hydrolysis of the anisidide, is not described in the literature. However, starting from the fact that chlorine is oriented in p-anisidides by both substituents (RSO_2NH and CH_3O groups) as is evident from the indicated equation for the hydrolysis, we suggest that in the case of o-anisidides as there occurs a similar orientation and therefore among all the six possible dichloro-o-anisidines, the one isolated by us has one of the two structures (I) or (II), of which (II) is more probable, since di-



(I)



(II)

chloro-o-anisidides of ethane- and butanesulfonic acids are difficultly soluble in alkali in contrast with all other N-arylamides, which fact may be explained by steric hindrance.

The compounds synthesized by us and the analytical data are in Table 1.

TABLE 1

Name of compound	Empirical formula	Analytical data (in %)					
		N		Cl		S	
		found	calc.	found	calc.	found	calc.
Ethanesulfodichloro-o-anisidide	$C_9H_{11}O_3NSCl_2$	4.87	4.92	25.14	24.95	11.31	11.27
Ethanesulfodichloro-p-anisidide	$C_9H_{11}O_3NSCl_2$	4.84	4.92	24.83	24.95	11.37	11.27
Ethanesulfotetrachloro-o-anisidide	$C_9H_9O_3NSCl_4$	4.16	3.96	40.75	40.0	9.15	9.06
Butanesulfodichloro-o-anisidide	$C_{11}H_{15}O_3NSCl_2$	4.46	4.51	22.85	22.93	8.28	8.35
Butanesulfotetrachloro-o-anisidide	$C_{11}H_{13}O_3NSCl_4$	3.68	3.77	38.0	37.27	7.20	7.08
Tetrachlorobenzoquinone	$C_6O_2Cl_4$	—	—	57.17	57.72	—	—
Dichloro-o-anisidine	$C_7H_7ONCl_2$	6.91	7.28	—	—	—	—
Dichloro-p-anisidide	$C_7H_7ONCl_2$	7.01	7.28	—	—	—	—

EXPERIMENTAL

Chlorination of o-anisidides of ethane- and butanesulfonic acids by means of gaseous chlorine. Into a suspension of 2 g of ethanesulfo-o-anisidide in 10 ml of carbon tetrachloride there was passed a stream of chlorine at the rate of 3-3.5 ml per second for 20 minutes at temperatures of 7° to 16°. Beginning 10-15 minutes after the start of the reaction there separated some small colorless crystals of the dichloroanisidide. The reaction mixture was left until the following day, when the crystals were separated, washed on the filter with carbon tetrachloride and dried. The yield was 1.91 g (74%); after crystallization from alcohol, m.p. 106-108°. From the filtrate left after the separation of the dichloroanisidide there was obtained a viscous oil after distillation of the carbon tetrachloride; this oil was treated with alcohol, whereby a finely crystalline precipitate of the tetrachloroanisidide formed which was separated, washed with alcohol and dried. The yield was 0.03 g (0.94%), m.p. 159-61° (from boiling alcohol). Change of the duration of chlorination from 20 to 60 minutes, as well as of the reaction temperature from 5° to 45° showed little effect on the course of the reaction and on the yields of the products formed. Running the reaction in the presence of zinc oxide lowered the yield of the dichloro products to 15-20%.

The o-anisidide of butanesulfonic acid was chlorinated in the same manner. From 1.5 g of the o-anisidide there was obtained 0.93 g (49%) of dichloro-o-anisidide with m.p. 144-145° (from alcohol).

Dichloro-o-anisidides of ethane- and butanesulfonic acids are readily soluble in benzene, glacial acetic acid, alcohol, carbon tetrachloride and ether which dissolve them on heating, and the substances crystallize out on cooling. The substances are soluble in dilute alkali only on heating and acidification of the alkaline solution leads to precipitation. Tetrachloroanisidides are soluble in alcohol only at the boiling point and are insoluble in alkali.

Chlorination of p-anisidides of ethane- and butanesulfonic acids by means of gaseous chlorine. The chlorination was run analogously to the above example. In case of ethanesulfo-p-anisidide there formed a crystalline dichloro-p-anisidide. The yield from 2 g of p-anisidide was 1.6 g; m.p. 163-165° (from alcohol). After distillation of carbon tetrachloride from the filtrate there remained a viscous yellow oil, from which there was isolated by treatment with boiling alcohol and subsequent cooling, some golden-yellow crystals of tetrachlorobenzoquinone (chloranil), m.p. 290° (from toluene). On mixing hot solutions in alcohol of tetrachlorobenzoquinone and aniline, a quantity of shiny brown crystals of dichlorodianilinobenzoquinone was isolated, which is a characteristic derivative of tetrachlorobenzoquinone [2].

In running the chlorination in the presence of zinc chloride, the yield of dichloroanisidide declines sharply; the same effect is observed in increased volume of the solvent. In chlorination of butanesulfo-p-anisidide the dichloro-p-anisidide was not isolated in a crystalline form. The above-described tetrachlorobenzoquinone, the yield of which in the various experiments ranged from 2.5 to 8.7%, was isolated from the oil formed as the result of distillation of carbon tetrachloride from the reaction mixture, this oil being then boiled with alcohol. The dichloro-p-anisidide of ethanesulfonic acid is soluble in hot benzene, alcohol and glacial acetic acid; it is insoluble in carbon tetrachloride and ether; it is soluble in cold dilute alkali and is precipitated from this solution by acids.

Chlorination of o- and p-anisidides of ethanesulfonic acid by a solution of chlorine. In this case chlorine was used in carbon tetrachloride solution calculated for molar ratios of the anisidide to chlorine equal to 1 : 1, 1 : 2, 1 : 3, and 1 : 4. Into 100 ml of carbon tetrachloride, previously weighed with the vessel, chlorine was added until the desired weight gain was reached, after which a recalculation was made for the content of chlorine per 1 ml of the solution. To a suspension of 2 g of the anisidide in 10 ml of carbon tetrachloride there was added the calculated volume of the chlorine solution. A boiling-up of the mixture and an abundant evolution of hydrogen chloride were observed while the reaction temperature rose to 30°, then slowly dropped to room temperature. In experiments with reactant ratios of 1 : 2, 1 : 3 and 1 : 4 a rapid formation of precipitate was observed, while in the experiment with 1 : 1 ratio no precipitate formed or only a very small one formed, this being, as shown by examination, a mixture of unreacted anisidide and the reaction products. A test for free chlorine with potassium iodide showed that in this experiment the free chlorine is absent after some 10-15 minutes. In remaining experiments the color with potassium iodide is seen even after two hours; in experiments with 1 : 3 and 1 : 4 ratios, some traces of chorine are detectable on the following day. In all cases the precipitates which formed as the result of the reaction were the dichloroanisidide, except for the experiment with 1 : 1 ratio

where, as indicated above, a considerable amount of unreacted anisidide was found in the precipitate along with dichloroanisidide. The separated crystals of dichloroanisidide were filtered from the reaction mixture on the following day, carbon tetrachloride was removed from the filtrate, and the residual oil was treated, as described above, and from it there was isolated tetrachloro-o-anisidide (in case of chlorination of o-anisidide - and of tetrachlorobenzoquinone) in case of chlorination of p-anisidide. The results of the chlorination by this technique are summarized in Table 2.

TABLE 2

Amount of chlorine taken (in g)	Molar ratio of starting materials	o-Anisidide chlorination; amount isolated (in %)		Isolated in chlorination of p-anisidide (in %)	
		dichloro-o-anisidide	tetrachloro-o-anisidide	dichloro-p-anisidide	tetrachloro-benzoquinone
0.66	1 : 1	Mixture of reaction products and starting materials			
1.32	1 : 2	53.7	3.0	25.0	—
1.98	1 : 3	52.2	4.2	40.1	5.2
2.64	1 : 4	56.8	4.2	43.9	7.0

Thus, chlorination with metered chlorine in solution leads to the same products which are formed in chlorination by unmetered chlorine in gaseous form; the yields of dichloroanisidides however are lower in this case while the yields of the by-products – tetrachloro-o-anisidides and tetrachlorobenzoquinone – are somewhat increased. Chlorination by means of a solution of chlorine was not run with o- and p-anisidides of butanesulfonic acid.

Hydrolysis of dichloroanisidides of ethane- and butanesulfonic acids. The corresponding anisidide (1.5 g) was heated to gentle reflux in 10 ml of dilute sulfuric acid (1 : 1) in a flask with a reflux condenser for several hours until a test sample became completely soluble in water. The mixture, after cooling, was diluted with one volume of water and was then made alkaline. Dichloroanisidine was extracted with ether. After drying with potassium carbonate, the ether was distilled. A viscous brown oil remained as the residue; this oil rapidly crystallized in the case of dichloro-o-anisidide, while in the case of dichloro-p anisidide it crystallized only after a treatment with alcohol, from which the hydrolysis product was precipitated by water.

SUMMARY

1. The reaction of chlorination of o- and p-anisidides of ethane- and butanesulfonic acids under various conditions was examined.

2. It was shown that under all conditions the main reaction products were dichloroanisidides, while the by-products for o-anisidides were tetrachloro-o-anisidides, and for p-anisidides the by-products consisted of tetrachlorobenzoquinone.

3. It was shown that in the reaction of chlorination of anisidides of alkanesulfonic acids, the alkylsulfonamido and the methoxy groups display an orienting effect in respect to chlorine to an equal degree.

4. It was shown that in hydrolysis of dichloroanisidides the corresponding dichloroanisidines are formed.

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INVESTIGATIONS IN THE FIELD OF QUINOLINE DERIVATIVES

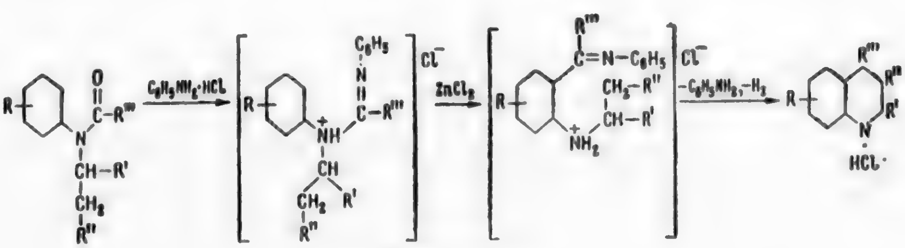
XIX. A NEW METHOD OF SYNTHESIS OF QUINOLINES BY REARRANGEMENT OF ACYLATED ARYLAMINES*

B. I. Ardashev and V.I. Minkin

Of the various rearrangement reactions of acylated anilines leading to the formation of aromatic aminoketones [1-7] special interest attaches to those rearrangements which ensue in cyclization with the formation of the heterocyclics -- acridine [8] and quinoline [9-11]. For this reason the rearrangement of N-ethylacetanilides into quinolines, known in the literature as the Pictet reaction [12], has in recent years been investigated in greater detail [13-15]. It has been found that addition to the starting materials – ethylacetanilide and zinc chloride – of salts of primary or secondary amines not only increases the yield of the quinoline derivatives, but also alters the cyclization mechanism leading to an interesting lepidine rearrangement [15].

In line with the extension of our work on the lepidine rearrangement of ethylacetanilides we have investigated rearrangements of a number of alkylformanilides which proceed in milder conditions in nitrobenzene as the solvent. The experimental data available indicate that the catalytic rearrangements of alkylacylanilides provide a means of preparing various homologs of quinoline and constitute one of a few methods of quinoline synthesis of a general character.

The mechanism of the rearrangement investigated differs from that of the Pictet reaction and does not involve the splitting off of an alkyl radical from the nitrogen atom, since α, β-dimethylindole, the formation of which might be expected in the latter case [13], does not form lepidine on interacting with aniline hydrochloride. As a result of investigations carried out it was established that the first stage of the reaction is the formation of N,N'-diaryl-N-alkyl-acylamidine which is obtained by heating amine salts with their acyl derivatives to a temperature of 150-160° [16, 17]. In point of fact, improved yields were obtained by using equivalent amounts of the amine salts; addition of salts of tertiary amines, which are incapable of yielding amidines, gave low yields of the final product of the rearrangement amounting to only 1-2% [4]. At elevated temperature, amidines rearrange into the anil of the corresponding o-aminocarbonyl compound which then undergoes cyclization into quinoline.



$R = H, CH_3, OCH_3$
$R', R'', R''' = H, CH_3$

* Communication XVIII, see [15].

The possibility of such a rearrangement is confirmed, firstly, by the formation of p-aminobenzaldehyde and p-aminoacetophenone on introducing aniline into the Goesch synthesis [18] with nitriles, in which case the intermediate product of the reaction is, evidently, N-phenylacylamidine which undergoes further isomerization [19]; a further confirmation is provided by our synthesis of quinoline from N-ethyl-N,N'-diphenylformamidine hydrochloride. Amidines possess a tendency to undergo rearrangements [20].

On the basis of the amidine rearrangement it is now possible to elucidate the hitherto obscure mechanism of the formation of flavaniline from acetanilide hydrochloride [21], of aminoacetophenones from acetanilide, in which case the presence of diphenylacetyamidine was detected among the reaction products [1], and of some other reactions.

EXPERIMENTAL

Preparation of starting materials. The starting alkylformanilides were prepared by the following methods: (a) by alkylation of formanilides with alkyl bromides in the presence of alcoholic KOH [22]; (b) by alkylation through the N-formyl-sodium derivatives of amines [23-25]; (c) by formylation of ethylanilines [26] in toluene [27]. The acetyl derivatives were prepared by interacting ethylanilines with acetic anhydride.

Preparation of quinoline derivatives. The rearrangement of the acetanilides was carried out by the method described earlier [15]; rearrangement of formanilides was effected by the following general method. The alkylformanilide (1 mole) was mixed with aniline hydrochloride (1 mole) and zinc chloride (1.1-1.4 mole) and the mixture was diluted with 5-6 times its weight of nitrobenzene and refluxed for 2-3 hours. The nitrobenzene was removed from the acid solution by steam-distillation, after which the bases were distilled from alkaline solution; tertiary amines were purified with phthalic anhydride [28] and subsequently distilled. The picrates were recrystallized from ethanolacetone solution, and after 1-2 recrystallizations had the required melting points. Only in the case of 6-methylquinoline was it necessary to purify the picrate through two cycles of the Manske treatment [29]. The results are listed in the Table.

Alkylacylanilide	Quinoline derivative (position and substituent	Boiling point	Yield (in %)	Melting point of picrate
Ethylformanilide	Quinoline	230—240°	11	198°
Isopropylformanilide	2-Methyl	*	4	188—189
n-Propylformanilide	3-Methyl	*	5	185
Ethylacetanilide [15]	4-Methyl	235—265	17	211—212
Ethylform-p-toluidide	6-Methyl	240—257	15	224
Ethylform-o-toluidide	8-Methyl	226—250	9	196
Ethylacet-p-toluidide[15]	4,6-Dimethyl	235—270	20	237
Ethylacet-o-toluidide	4,8-Dimethyl	93—100 (5 мм)	14	214—215
Ethylform-m-xylidide	6,8-Dimethyl	90—106 (5 мм)	12	226—227
Ethylacet-m-xylidide	4,6,8-Trimethyl	*	6	206
Isopropylform-m-xylidide	2,6,8-Trimethyl	250—270	5	184—186
Ethylform-p-anisidide	6-Methoxy	240—265	18	209
Methylacet-p-anisidide**	6-Methoxy	*	2	205

* Isolated as the picrate.

** Reaction proceeds by the indole mechanism [13].

Quinoline from N-ethyl-N,N'-diphenylformamidine. Amidine was prepared by heating 17.5 g of formethylaniline and 15.4 g of aniline hydrochloride at 150° under reduced pressure for $1\frac{1}{2}$ hours. To the semi-solid mass, constituting the amidine salt, was added 17 g of $ZnCl_2$ and 85 ml of nitrobenzene and the mixture was refluxed for 2 hours. Yield of the quinoline, 1.5 g (10%), b.p. 225-240°. The picrate, formed in alcohol, melts at 191°, and after recrystallization from acetone, at 199°. Mixture of this picrate with an authentic sample did not depress the melting point; the same applies to all other quinolines listed in the Table.

The following compounds have not so far been described in the literature: ethylform-o-toluidide (b.p. 255-265°), ethylform-p-toluidide (b.p. 142°, 4 mm), ethylform-m-xylidide (b.p. 265-270°), ethylacet-m-xylidide

(b.p. 265°), ethylform-p-anisidide (b.p. 160-175°, 7 mm), isopropylform-m-xylidide (b.p. 260-275°) and N-ethyl-N,N'-diphenylformamidine hydrochloride (m.p. 150-154°).

SUMMARY

1. The rearrangement of a number of alkylacylanilides in the presence of aniline hydrochloride has been investigated.

2. The general nature of this reaction and its use in the synthesis of various quinoline derivatives has been demonstrated.

3. It has been established that the mechanism of the reaction involves the formation of N-alkyl-N,N'-diarylamidines as intermediate products.

4. The reaction investigated is an entirely novel method of synthesis of quinoline derivatives.

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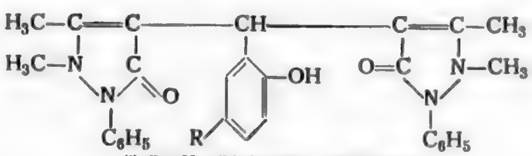
INTERACTION OF AQUEOUS SOLUTIONS OF SALTS OF TETRAVALENT TITANIUM WITH PYRAZOLONE DERIVATIVES

R. G. Beiles*

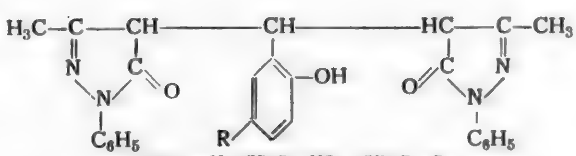
Earlier we have established that during the interaction of aqueous solutions of salts of Ti^{4+} with diantipyryl-o-hydroxyphenylmethane (I) there appears an orange-yellow coloration, or else there are formed precipitates of unknown composition [1].



(I) R=H, (II) R=NO_2, (III) R=Br.

It has now been found that not only compound (I), but also some other products of the interaction of salicylaldehyde with pyrazolone derivatives react readily with titanic ions; the reaction products may be obtained in the form of well-defined crystalline compounds. Below are described results of an investigation of the interaction of titanium ions with bis-pyrazolone derivatives of salicylaldehyde.

1. Interaction of Ti^{4+} ions with dipyrazolonyl-o-hydroxyphenylmethane and its derivatives. (a) Interaction in the presence of weakly basic compounds. If a solution of CH_3COONa, K_2CO_3, urotropine or of some other weakly-basic compound is added to an acid aqueous-alcoholic solution containing $TiCl_4$ and dipyrazolonyl-o-hydroxyphenylmethane (IV), there is formed an orange-colored precipitate (Fig. 1). Precipitation takes place at a pH of 3 to 5.



(IV) R=H, (V) R=NO_2, (VI) R=Br.

An interesting property of this substance is its exceptional stability, characteristic of titanium derivatives, towards the action of NaOH, KOH and other alkalis. The compound is also stable towards the action of concentrated phosphoric acid.

Analysis has shown that one atom of Ti is combined with two molecules of compound IV; the composition of the substance may be represented by the formula 2 DipTi=O, where Dip represents dipyrazolonyl-o-hydroxyphenylmethane.

In a similar manner were obtained titanium derivatives containing a nitro group (from compound V) and a bromine atom (from compound VI) in the benzene nucleus.

* With the collaboration of N. G. Trotsenko, M. A. Timchenko, A. L. Russkii, and Iazova, all students at the Upper-Altai Teachers' Training Institute.

Compounds Formed as a Result of Interaction of bis-Pyrazolone Derivatives with Ti^{4+} Ions in Aqueous-Alcoholic Solutions (The table gives the color of the substance, microscopic appearance of the crystals and the decomposition temperature*)

Starting bis-pyrazolone derivatives	Result on addition of weak-base	Reaction conditions							
		Result on addition of inorganic salts							
		KCl	KI	KNO_3	$KClO_3$	NH_4ClO_4	KCNS	K_2SO_4	$K_2S_2O_8$
(IV)	Red, rectang. prisms and rombi, 265°	Red, cubes, 275°	Red, cubes and octahedrons, 220°	Orange prisms 240°	Orange, cubes, 130°	Orange, cubes and prisms, 210°	Red, fine cubes, 250°	Organge, prisms, 230°	Red, prisms and cubes, 250°
(V)	Orange, prisms, decomposes above 350°	Orange, prisms, 250°	Red, prisms, and plates, 230°	Orange, prisms, 215°	Orange, prisms, 300°	Orange, rombi and plates, 240°	Red, prisms and plates, 210°	Orange, fine prisms, decomp. above 350°	Orange, prisms and plates, decomp. above 350°
(VI)	Red, X-shaped dendrites, 295°	Yellow, needle clusters and prisms, 290°	Red, prisms and cubes, 300°	Orange, prisms, 315°	Orange prisms, 285°	Yellow, 270°	Red prisms and cubes, 265°	Orange, fine prisms, decomp. above 350°	Orange, prisms, decomp. above 360°
(I)	No reaction	Orange, prisms, 240°	Red, needle clusters, 270°	Orange, needles, 285°	Orange, needle clusters, 230°	Orange, fine needles, 280°	Red, needle clusters, 220°	—	—
(II)	No reaction	—	Orange, needles or prisms, 240°	Yellow, needle clusters, 260°	Yellow, needle clusters, 230°	Orange, needles or prisms, 260°	Red, needles or prisms, 230°	—	—
(III)	No reaction		Red, needle clusters, 280°	Orange, needle clusters, 290°	Orange, prisms, 260°	Orange, prisms, 280°	Red, prisms, 230°	—	—
		Compounds 2DTI=O	Compounds $2DTiX_2$						

*Fusion and decomposition comes about gradually; the table gives the temperature at which a noticeable change begins.

Fig. 1. Crystals of the compound 2 Dip Ti=O (x 140).

Fig. 2. Crystals of the compound 2 Diant $Ti(NO_3)_2$. (x 140).

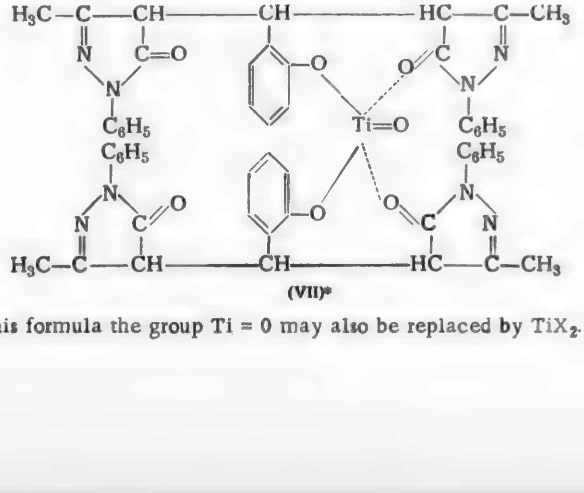
(b) Interaction of Ti^{4+} ions with dipyrazolonyl-o-hydroxyphenylmethane in the presence of various salts. Crystalline precipitates may also be obtained from solutions containing Ti^{4+} and dipyrazolonyl-o-hydroxyphenylmethane even in the absence of weak bases; namely, on addition of salts of the most anions (X). Analyses have shown that the composition of the precipitates may be expressed by the formula 2 Dip TiX_2. Our investigations included precipitates in which X was Cl, I, NO_3, ClO_3, ClO_4, CNS, S_2O_8, as well as some other anions (see Table). The compounds resemble in many respects those described above. Analogous titanium derivatives containing a nitro group (from compound V) and a bromine atom (from compound VI) have also been prepared.

Thus, dipyrazolonyl-o-hydroxyphenylmethane and its derivatives form two series of compounds with tetravalent titanium represented, respectively, by the formulas 2 Dip Ti=O and 2 Dip TiX_2.

2. Interaction of Ti^{4+} ions with diantipyryl-o-hydroxyphenylmethane and its derivatives. Diantipyryl-o-hydroxyphenylmethane (I) and its nitro and bromo derivatives (II and III) react with Ti^{4+} in the presence of various salts in a manner similar to the reaction of these ions with dipyrazolonyl-o-hydroxyphenylmethane (see par. 16) giving crystalline precipitates of the composition 2 Diant TiX_2 (see Fig. 2). This reaction was used by us in a quantitative estimation of titanium [2].

The precipitates are decomposed gradually, over a period of several hours, by solutions of alkali, with the formation of titanium hydroxide. The derivative in which X = I, reacts only very slowly with $AgNO_3$ solution.

In contrast to dipyrazolonyl-o-hydroxyphenylmethane (IV), compounds I to III do not form derivatives of the type which might be represented by 2 Diant Ti=O, i.e. the reaction does not proceed in the presence of weak bases. This difference in behavior is apparently due to the presence in compound (IV) of a labile hydrogen atom owing to which the compound exhibits amphoteric properties; the compound dissolves in alkalis with the formation of its enolic form [3]. By contrast, compound (I) does not undergo a similar tautomeric transformation.

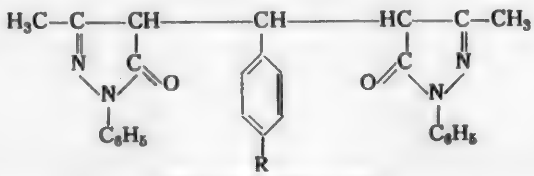


(VII)*

*In the central portion of this formula the group Ti = 0 may also be replaced by TiX_2.

The properties of the compounds obtained and, in particular, their stability towards the action of alkalis indicate that the titanium atom is linked by complex-type bonds to the molecules of bis-pyrazolone compounds. In view of this, these compounds may be represented by the structural formula (VII) [in the case of those derived from compound (IV)].

The formulas proposed may be comfirmed to some extent by the following facts. If the OH group in the benzene ring is absent [as in dipyrazolonyl-phenylmethane (VIII) or diantipyrylphenylmethane], the reaction with titanium does not occur.



(VIII) R=H; (IX) R=OH.

No reaction will take place, either, if the OH group is in the para-position [dipyrazolonyl-p-hydroxyphenylmethane (IX) and diantipyryl-p-hydroxyphenylmethane]. Consequently, the presence of the hydroxy group in the ortho-position is a prerequisite for reaction with titanium. However, the data available are still insufficient in order to establish definitely the structure of these compounds.

EXPERIMENTAL

1. Preparation of bis-pyrazolone derivatives. Compounds (I-VI, VIII-IX) were prepared by the method described earlier for diantipyryl-o-hydroxyphenylmethane [1] with certain modifications in each case. The separations into "white" and "yellow" isomers [3] were not carried out.

Diantipyryl-2-hydroxy-5-nitrophenylmethane (II) was obtained from antipyrine and 5-nitrosalicylaldehyde as a white substance melting at 268-270° (for the free base).

Found %: C 65.94; H 5.06; N 13.06; $C_{29}H_{27}O_5N_5$. Calculated %: C 66.29; H 5.18; N 13.33.*

Diantipyryl-2-hydroxy-5-bromophenylmethane (III) was prepared from antipyrine and 5-bromosalicylaldehyde; white substance melting at 269-271°. The hydrochloride melts at 149-150°

Found %: N 9.89; Br 14.01. $C_{29}H_{27}O_3N_4Br$. Calculated %: N 10.01; Br 14.28.

Diantipyryl-p-hydroxyphenylmethane was prepared from antipyrine and p-hydroxybenzaldehyde [1].

Dipyrazolonyl-2-hydroxy-5-nitrophenylmethane (V) was obtained from 1-phenyl-3-methylpyrazolone-5 and 5-nitrosalicylaldehyde as a yellow to orange substance, m.p. 220-222°.

Found %: C 64.86; H 4.38; N 14.04. $C_{27}H_{23}O_5N_5$. Calculated %: C 65.18; H 4.66; N 14.07.

Dipyrazolonyl-2-hydroxy-5-bromophenylmethane (VI) was obtained from 1-phenyl-3-methylpyrazolone-5 and 5-bromosalicylaldehyde. Light yellow substance, m.p. 228-230°.

Found %: N 10.41; Br 14.76. $C_{27}H_{23}O_3N_4Br$. Calculated %: N 10.55; Br 15.04.

Dipyrazolonyl-p-hydroxyphenylmethane (IX), m.p. 159-160° [3]; dipyrazolonylphenylmethane (VIII), m.p. 227-229° [4]; dipyrazolonyl-o-hydroxyphenylmethane (IV) was obtained as a yellowish-white substance melting at 220-222° [3].

2. Preparation of titanium derivatives of the composition 2DipTi=O. To 200 ml of 2% alcoholic solution of compound (IV) was added 20 ml of 1% $TiCl_4$ solution in dilute HCl. The mixture developed an orange-red coloration. Whenever necessary the solution was filtered to remove a small amount of a precipitate and to the

* Determinations of nitrogen were carried out in the Laboratory of Organic Chemistry of the Ural Polytechnical Institute.

filtrate was added a 10% aqueous solution of urotropine until a copious yellow precipitate formed. In place of urotropine, solutions of CH_3COONa, K_2CO_3, potassium citrate and other weakly-basic substances may be used. The mixture was heated to reflux; on cooling the yellow precipitate changed in color to an orange-red. After washing with water, alcohol and ether there was obtained 3.0 g of the titanium derivative (for microscopic view of the crystals see Fig. 1).

The substance is sparingly soluble in alcohol and acetone, slightly more soluble in dioxane and pyridine. In dilute and concentrated solutions of NaOH and KOH it forms orange-colored solutions which are stable in the cold; on acidifying these alkaline solutions the compound precipitates unchanged. On boiling the alkaline solution there occurs hydrolysis with the formation of TiO_2 and dipyrazolonyl-o-hydroxyphenylmethane. Solution of the compound in NH_4OH is unaffected on boiling. Above 265° the compound decrepitates with decomposition.

Found %: C 66.75; H 4.64; N 11.13; Ti 5.07. $C_{64}H_{46}O_7N_8Ti$. Calculated %: C 67.07; H 4.80; N 11.58; Ti 4.95.

The titanium derivatives of compounds (V) and (VI) were obtained in a manner similar to that described above (see Table).

3. Preparation of titanium derivatives of the composition $2DTiX_2$. From compounds (I-VI) and $TiCl_4$ were obtained aqueous-alcohol solutions of the titanium derivatives, as described in section 2 above. To the reaction mixture was added a 5-10% solution of KI, KNO_3 or of some other salt, depending on the nature of the radical X to be introduced into the molecule.* Addition of certain salts for example, of $K_2S_2O_8$, induces a distinct crystallization process in the cold. The derivatives of dipyrazolonyl-o-hydroxyphenylmethane and of its analogs (IV-VI) resemble in their properties the products of the type 2DipTi=O described above.

Derivatives of diantipyryl-o-hydroxphenylmethane (I-III) differ from the other derivatives in their lower stability towards alkalis (slow hydrolysis in the cold) as well as in their considerably lower solubility and good crystallizing properties, particularly in the case NO_3 and ClO_3 derivatives [2].

The results of the analysis of the derivative obtained from diantipyryl-o-hydroxyphenylmethane (I), with X = I, are given below as an example:

Found %: N 8.73; 20.04; Ti 3.85. $C_{58}H_{54}O_6N_8I_2Ti$. Calculated %: N 8.89; I 20.13; Ti 3.80.

The compounds prepared are listed in the Table.

SUMMARY

Interaction of aqueous solutions of salts of tetravalent titanium with bis-pyrazolone derivatives of salicylaldehyde (D) gives rise to the formation of compounds having the composition 2 DTi=O and 2 $DTiX_2$, where X = Cl, I, NO_3 and other radicals. 40 compounds of both types have been prepared and a few hitherto unknown bis-pyrazolone derivatives have been described.

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* Compounds in which X = Cl may be precipitated from the solution by the addition of water, or they may be obtained by evaporating the solution without the addition of any reagents.

ANILIDES OF ALKYLSULFONAMIDOPHOSPHORIC ACIDS

A. V. Kirsanov and N. L. Egorova

The action of aniline on trichlorophosphazosulfonalkyls [1] might be expected to give anilidodichlorophosphazosulfonalkyls of the type $RSO_2N=PCl_2(NHC_6H_5)$ (I), dianilidochlorophosphazosulfonalkyls of the type $RSO_2N=PCl(NHC_6H_5)_2$ (II), and trianilidophosphazosulfonalkyls of the type $RSO_2N=P(NHC_6H_5)_3$. But type (I) substances were not obtained (Cf. [2]). Even with a large excess of the trichlorophosphazosulfonalkyl it was impossible to isolate any of (I) from the reaction products. Dianilidochlorophosphazosulfonalkyls (II) were obtained in satisfactory yields by the reaction of trichlorophosphazosulfonalkyls with aniline in carbon tetrachloride solution. These were found to be colorless crystalline substances of neutral character, easily hydrolyzed to dianilides of alkylsulfonamidophosphoric acids (III), by heating their solution in 96% alcohol, or by boiling with water, according to the equation

$$RSO_2N{=}PCl(NHC_6H_5)_2 + H_2O \rightarrow HCl + \underset{\text{(III)}}{RSO_2NHPO(NHC_6H_5)_2}$$

Readily soluble salts of III were formed by the action of aqueous solutions of caustic alkalis and ammonia on II. Free III was precipitated on acidification of a solution of the salt; for this reason it was not necessary to isolate II in the preparation of III – it was sufficient to treat the reaction mixture with sodium hydroxide solution, and subsequently isolate III.

III salts were found to be colorless crystalline substances, with a very bitter taste, and were not hydrolyzed even by prolonged boiling with water or alkali solutions. They were slowly hydrolyzed on heating with dilute mineral acids to form the amides ofalkylsulfonic acids and the anilides of phosphoric acid. They were fairly strong monobasic acids.

The trianilidophophazosulfonalkyls (IV) were obtained in good yield by the prolonged heating of trichlorophosphazosulfonalkyls with excess of aniline in benzene solution. They were found to be colorless crystalline substances, with a bitter taste, of a neutral character and very resistant to the action of alkali (cf. [3]). They remained unchanged even after prolonged boiling with alcoholic alkali. The other properties of substances II to IV are given in the experimental part.

EXPERIMENTAL

Dianilidochlorophosphazosulfonethyl (V). A solution of 0.05 mole of freshly distilled aniline in 15.0 ml of CCl_4 was added slowly, with vigorous stirring, to a solution of 0.01 mole of trichlorophosphazosulfonethyl in 15.0 ml of dry CCl_4. The reaction was accompanied by the liberation of a large amount of heat; so the reaction mixture was cooled by water and ice, to maintain the temperature between 5 and 15°. If the reaction was carried out at a higher temperature, a considerable quantity of trianilidophosphazosulfonethyl was formed, and the yield of V was reduced. The reaction mixture was allowed to stand for two days at room temperature, after which the mixture of V and aniline hydrochloride was filtered off under suction, and the V was extracted with boiling benzene. The V crystallized out from the cold benzene solution in the form of agglomerates of transparent prisms. Yield 60.2%, m.p. 88-89°.

Found %: N 11.59; equiv. after hydrolysis, 1.99, 1.97. $C_{14}H_{17}O_2N_3SPCl$. Calculated %: N 11.78. equiv. after hydrolysis, 1.00.

V was readily soluble in acetone and dioxane, and readily soluble on heating in benzene, ether, petroleum ether, carbon tetrachloride and ethyl acetate.

Dianilidochlorophosphazosulfon-n-butyl (VI) was readily soluble in CCl_4. After carrying out the reaction and filtering off the aniline hydrochloride, the filtrate was evaporated on a water bath under reduced pressure, and the residue was washed with a small amount of cold benzene to remove excess aniline, and recrystallized from boiling benzene, if necessary with the addition of active carbon. VI consisted of fine prisms, m.p. 176-178°, yield 65.3%.

Found %: N 11.15. $C_{16}H_{21}O_2N_3SPCl$. Calculated %: N 10.90.

VI was readily soluble in acetone, dioxane and carbon tetrachloride, and with considerable difficulty in benzene, ether, petroleum ether, and ethyl acetate. V and VI gave VII and VIII (see below) on heating with alcohol, or by the action of caustic alkali solutions.

Dianilide of ethylsulfonamidophosphoric acid (VII). A mixture of 0.01 mole of V and 40.0 ml of N aqueous caustic soda was heated to boiling and filtered, and the hot solution was treated with 5N hydrochloric acid until acid to congo red. The crystalline hydrate of VII then precipitated in the form of fine colorless prisms Yield 62.2%, m.p. 127-130°.

Found %: H_2O 2.59. $(C_{14}H_{18}O_3N_3SP)_2 \cdot H_2O$. Calculated %: H_2O 2.58.

The crystalline hydrate was completely freed from water by heating to 100°, or by recrystallization from benzene. Anhydrous VII crystallized from benzene in the form of fine needles, m.p. 158-160°.

Found %: N 12.49. Equiv. 1.006, 0.993. $C_{14}H_{18}O_3N_3SP$. Calculated %: N 12.39. Equiv. 1.000.

Dianilide of n-butylsulfonamidophosphoric acid (VIII). This was obtained in the same way as VII. Yield 59.9%, m.p. 188-89°. Fine thin prisms (from water).

Found %: N 11.33, 11.23. Equiv. 0.99, 1.010. $C_{16}H_{22}O_3N_3SP$. Calculated %: N 11.44. Equiv. 1.000.

VII and VIII had a very bitter taste. They were readily soluble in acetone, dioxane, alcohol and ethyl acetate and they were soluble in hot water and benzene, and with great difficulty in CCl_4 and petroleum ether. VII and VIII could be obtained without the isolation of V and VI in the pure state. To do this, the crude intermediates were treated with a hot solution of caustic soda, the solution was decolorized with active carbon, and VII and VIII were precipitated with hydrochloric acid.

Trianilidophosphazosulfonethyl (IX). A solution of 0.01 mole of trichlorophosphazosulfonethyl in 10.0 ml of dry benzene was added to a solution of 0.08 mole of freshly distilled aniline in 10.0 ml of benzene, with stirring and cooling (much heat was liberated). The reaction mixture was then boiled under reflux on a water bath for 10 hours. The precipitated mixture of IX and aniline hydrochloride was filtered under suction, and washed with benzene, a few times with water, with N hydrochloric acid, with 0.5 N sodium hydroxide (to remove VII) and again with water. Yield 79.0%, m.p. 251-252°, crystallized from alcohol as long needles.

Found %: N 13.66. $C_{20}H_{23}O_2N_4SP$. Calculated %: N 13.53.

Trianilidophosphazosulfon-n-butyl (X). This was obtained in the same way as IX. Yield 78.6%, m.p. 232-233°; crystallized from benzene or alcohol in the form of small needles.

Found %: 12.44. $C_{22}H_{27}O_2N_4SP$. Calculated %: N 12.66.

IX and X had a bitter taste, and were insoluble in water or aqueous solutions of caustic alkali or acid. They dissolved on heating in acetone, dioxane, alcohol and ethyl acetate, but were insoluble in CCl_4 and petroleum ether.

SUMMARY

Dianilidochlorophosphazosulfonalkyls, trianilidophosphazosulfonalkyls and dianilides of alkylsulfonamidophosphoric acids have been prepared and their properties have been described.

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SALTS OF THE ACID FLUORIDES OF ARYLSULFONAMIDO-PHOSPHORIC ACIDS

A. V. Kirsanov and E. S. Levchenko

The readily available and sufficiently studied trichlorophosphazosulfonaryls [1] and the products of their hydrolysis, the acid dichlorides of arylsulfonamidophosphoric acids [2], are very reactive compounds and can be used as starting materials for the synthesis of various new organic phosphorus compounds [3]. Considerable interest attaches to the investigation of fluorine compounds analogous to the trichlorophosphazosulfonaryls and to the acid dichlorides of arylsulfonamidophosphoric acids. Attempts to replace chlorine by fluorine in the latter, using sodium or potassium fluorides in neutral organic solvents, did not meet with success. Antimony trifluoride was also found to be unsuitable for this purpose, as it was impossible to isolate the individual products from the reaction mixture.

It is known that chlorine is readily replaced by fluorine in various acids in reactions with aqueous solutions of potassium fluoride or bifluoride; for example, the acid dichlorides of the diethylamides of phosphoric and thiophosphoric acids, when heated with a saturated aqueous solution of potassium fluoride, give the corresponding acid fluorides [4]. Heat was liberated when trichlorophosphazosulfonaryls reacted with a saturated aqueous solution of potassium fluoride. In this reaction, besides the replacement of chlorine atoms by fluorine, there was partial hydrolysis leading to the formation of potassium salts of the acid difluorides of arylsulfonamidophosphoric acids, according to the over-all scheme:

$$AsSO_2N{=}PCl_3 + 6KF + H_2O \rightarrow K^+(ArSO_2NPOF_2)^- + 3KCl + 2KHF_2$$

The same compounds were obtained by the interaction of the acid dichlorides of arylsulfonamidophosphoric acids with an aqueous solution of potassium fluoride, according to the over-all scheme:

$$ArSO_2NHPOCl_2 + 4KF \rightarrow K^+(ArSO_2NPOF_2)^- + 2KCl + KHF_2$$

In this case the reaction was less vigorous, and it was necessary to heat the reaction mixture to 30-40°.

The reaction of the formation of the potassium salts of the acid difluorides of arylsulfonamidophosphoric acids passed through the stage of the potassium salts of the acid dichlorides of the arylsulfonamidophosphoric acids, $ArSO_2NKPOCl_2$ [5], which then exchanged chlorine for fluorine. This was shown by the interaction of the acid dichloride of phenylsulfonamidophosphoric acid with potassium fluoride solution at room temperature, when the potassium salt of the acid dichloride was formed in good yield, and chlorine was readily replaced by fluorine in this, by interaction with potassium bifluoride solution.

$$K^+(C_6H_5SO_2NPOCl_2)^- + 2KHF_2 \rightarrow K^+(C_6H_5SO_2NPOF_2)^- + 2KCl + 2HF$$

This reaction did not take place with a neutral solution of potassium fluoride. Thus the replacement of chlorine by fluorine in the acid dichlorides of arylsulfonamidophosphoric acids occurs by the action of the HF_2^- ion, and not of the F^- ion, i.e. according to the equation:

$$ArSO_2N{=}PCl_3 + H_2O + 4KF \rightarrow K^+(ArSO_2NPOCl_2)^- + KCl + 2KHF_2 \text{ etc.}$$
$$ArSO_2NHPOCl_2 + 2KF \rightarrow K^+(ArSO_2NPOCl_2)^- + KHF_2 \text{ etc.}$$

The potassium salts of the acid difluorides of phenyl-, p-tolyl-, p-chlorophenyl, p-fluorophenyl- and o-, m- and p-nitrophenylsulfonamidophosphoric acids were obtained by the reaction of trichlorophosphazosulfonaryls with aqueous solutions of potassium fluoride. The products obtained were colorless crystalline compounds, with properties recalling those of the acid dichlorides of the arylsulfonamidophosphoric acids [5]. They are readily soluble in water, with difficulty in methyl and ethyl alcohols, and insoluble in benzene and ether. The potassium salts of the acid difluorides were even more resistant to hydrolysis than those of the acid difluorides. For example, the potassium salts of the acid difluorides could be recrystallized from water heated to 70-80°, though they were hydrolyzed quite rapidly when their aqueous solutions were boiled.

The potassium salts of the acid difluorides of arylsulfonamidophosphoric acids behaved like the salts of the acid dichlorides in reacting with sodium methylate, to give good yields of the methyl esters of the arylsulfonamidophosphoric acids, and this clearly establishes their structures.

$$K^+(ArSO_2NPOF_2)^- + 2CH_3ONa \rightarrow 2NaF + K^+[ArSO_2NPO(OCH_3)_2]^- \xrightarrow[HCl]{}$$
$$\longrightarrow KCl + ArSO_2NHPO(OCH_3)_2$$

When the potassium salts of the acid difluorides of arylsulfonamidophosphoric acids were heated with potassium fluoride solution, until they had dissolved completely (80-85°), they were partly hydrolyzed to give the dipotassium salts of the acid monofluorides. If the reaction mixture for the fluorination of the acid dichlorides, or of the trichlorophosphazosulfonaryls, was carefully heated on a water bath until the products of the first stage of fluorination (the potassium salts of the acid difluorides) had dissolved, then, on cooling, the dipotassium salts of the acid monofluorides of the arylsulfonamidophosphoric acids separated out in the form of crystalline precipitates. The reaction is as follows:

$$ArSO_2NHPOCl_2 + 7KF + H_2O \rightarrow K_2^+(ArSO_2NPO_2F)^{--} + 2KCl + 3KHF_2.$$

In this way we obtained the dipotassium salts of the acid monofluorides of the p-chlorophenyl-, and o-, m- and p-nitrophenylsulfonamidophosphoric acids. These were colorless crystalline substances, very readily soluble in water and insoluble in organic solvents. The corresponding silver salts were less soluble in water.

The remarkable resistance to hydrolysis, in neutral and alkaline aqueous solution, of the salts of the acid dichlorides [5] and acid difluorides of arylsulfonamidophosphoric acids, of the type $K^+(ArSO_2NPOX_2)^-$ is probably due to the influence of the electronegative substituent $(ArSO_2N)^-$ on the phosphorus atom. Similar cases are described in the literature. For example, it is difficult to hydrolyze the acid dichloride of triphenylmethylphosphinic acid $(C_6H_5)_3CPOCl_2$ [6], or the acid monochloride of trichloromethylphosphinic acid [7], and fairly difficult to hydrolyze the acid dichlorides of arylsulfonamidophosphoric acids $ArSO_2NHPOCl_2$ [2] and the acylamidophosphoric acids $AcNHPOCl_2$ [8]. It is well known that acid dichlorides of phosphoric acids, in which there is no electronegative group attached to the phosphorus atom, hydrolyze very easily. The lower resistance to hydrolysis of the free acid dichlorides of arylsulfonamidophosphoric acids, compared with their salts, is probably due to the greater electronegativity of the $(ArSO_2N)^-$ substituent than of $(ArSO_2NH)$. For the same reason, CCl_3POCl_2 hydrolyzes considerably more easily than $CCl_3PO(OH)Cl$ [7].

EXPERIMENTAL

Potassium salts of arylsulfonamidophosphoric acids from trichlorophosphazosulfonaryls. The finely divided trichlorophosphazosulfonaryl (0.01 mole) was added, with stirring, to a saturated aqueous solution of 10.0 g of crystalline potassium fluoride ($KF \cdot 2H_2O$). The temperature rose to 30-40°, and, after a few minutes, the residual trichlorophosphazosulfonaryl was converted into a colorless crystalline deposit of the corresponding potassium salt. Dissolution did not take place, but the form of the new deposit was so characteristic that there was not difficulty in detecting the end of the reaction. After cooling, the product was filtered off under suction, pressed between sheets of filter paper, dried in air and recrystallized. Yields were determined for the pure products (see Table 1).

Potassium salts of the acid difluorides of phenyl and p-tolylsulfonamidophosphoric acids from acid dichlorides of the corresponding arylsulfonamidophosphoric acids. A suspension of 0.01 mole of the acid dichloride of the arylsulfonamidophosphoric acid in a saturated solution of 10.0 g of potassium fluoride was heated on a water bath to 30-40°. Dissolution did not occur under these conditions, but the form of the deposit changed markedly and, after a few minutes, crystals of the original substance disappeared as they were converted into a deposit of

TABLE 1

Potassium Salts of Acid Difluorides of Arylsulfonamidophosphoric Acids of the Type $K^+(ArSO_2NPOF_2)^-$

Aryl	Crystalline form	Solvent for crystallization	Melting point	Yield (%)	Formula	Found, %			Calculated %		
						N	K	F	N	K	F
C_6H_5	Colorless, lustrous, fine platelets	Ethanol or water	230—232°	52.0	$C_6H_5O_3NSPF_2K$	4.95, 5.14	14.08, 14.90	14.20, 14.53	5.01	13.62	13.96
$p\,CH_3C_6H_4$	Platelets	Methanol	232—235	61.0	$C_7H_7O_3NSPF_2K$	5.04, 5.06	—	13.37, 13.05	4.77	—	12.96
p-ClC_6H_4	Platelets	Ethanol or water	265—268	57.0	$C_6H_4O_3NSPClF_2K$	4.20, 4.33	12.20, 12.60	13.14, 12.74	4.46	12.44	12.12
p-FC_6H_4	Platelets	Ethanol	225—228	35.3	$C_6H_4O_3NSPF_3K$	—	—	19.70	—	—	19.19
o-$NO_2C_6H_4$	Needles	Ethanol	181—182	40.7	$C_6H_4O_5N_2SPF_2K$	8.67, 8.68	—	—	8.64	—	—
m-$NO_2C_6H_4$	Platelets	Ethanol or water	217—220	61.0	$C_6H_4O_5N_2SPF_2K$	8.19, 8.25	—	—	8.64	—	—
p-$NO_2C_6H_4$	Platelets Needles	Aqueous, ethanol, water	225—228	58.0	$C_6H_4O_5N_2SPF_2K$	8.52, 8.60	—	—	8.64	—	—

the potassium salt. After cooling, the fine colorless crystals of the potassium salt were filtered off under suction and recrystallized from alcohol. The product had the same melting point, and gave no mixed melting point depression with the potassium salt of the acid difluoride of the arylsulfonamidophosphoric acid prepared from the corresponding trichlorophosphazosulfonaryl. The salts were obtained in 40 and 30.7% yields respectively.

Potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid from the acid dichloride of phenylsulfonamidophosphoric acid and potassium fluoride (without heating). The acid dichloride of phenylsulfonamidophosphoric acid (0.01 mole) was added, with vigorous stirring, to a saturated solution of 10.0 g of potassium fluoride, and the reaction mixture was stirred carefully for a further 20 minutes. Dissolution did not occur, but the external form of the deposit changed markedly (see above). The crystalline deposit was filtered off under suction, pressed but not dried, and recrystallized from alcohol. Yield 48.0%. The product was in the form of colorless needles, of m.p. 197-198°, and gave no mixed melting point depression with the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid, obtained by the action of potash on the acid dichloride of phenylsulfonamidophosphoric acid [5].

Potassium salt of the acid difluoride of phenylsulfonamidophosphoric acid from the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid and potassium bifluoride. A mixture of 0.005 mole of the potassium salt of the acid dichloride of phenylsulfonamidophosphoric acid with a saturated aqueous solution of 3.0 g of potassium bifluoride was carefully heated on a water bath at 40-50°, until dissolution was complete. After cooling, the product was filtered off under suction and recrystallized from alcohol. Yield 86.0%, m.p. 230-232°. The substance gave no mixed melting point depression with the potassium salt of the acid difluoride of phenylsulfonamidophosphoric acid obtained from trichlorophosphazosulfonphenyl.

TABLE 2

Dimethyl Esters of Arylsulfonamidophosphoric Acids of the Type $ArSO_2HNPO(OCH_3)_2$

Aryl	Yield,%	Melting point	Literature reference
C_6H_5	46.0	106-108°	[9]
$p\text{-}ClC_6H_4$	68.0	128-129	[5]
$m\text{-}NO_2C_6H_4$	63.0	149-150	[10]
$p\text{-}NO_2C_6H_4$	68.0	177-179	[10]

Dimethyl esters of arylsulfonamidophosphoric acids. A suspension of 0.005 mole of the potassium salt of the acid difluoride of the arylsulfonamidophosphoric acid in 5.0 ml of methanol was treated with a solution

TABLE 3

Dipotassium Salts of Acid Monofluorides of Arylsulfonamidophosphoric Acids of the Type $K_2^{+}(ArSO_2NPO_2F)^{--}$

Aryl	Melting point	Yield (in %)	Formula	Found, %			Calculated,%		
				N	K	F	N	K	F
$p\text{-}ClC_6H_4$	312—316°	46.0	$C_6H_4O_4NSPClFK_2$	—	21.45	6.35	—	22.31	5.43
$o\text{-}NO_2C_6H_4$	235—237	77.0	$C_6H_4O_6N_2SPFK_2$	7.85, 7.75	—	—	7.77	—	—
$m\text{-}NO_2C_6H_4$	302—306	73.0	$C_6H_4O_6N_2SPFK_2$	8.03, 8.04	—	5.69, 5.94	7.77	—	5.27
$p\text{-}NO_2C_6H_4$	299—302	37.0	$C_6H_4O_6N_2SPFK_2$	7.74, 7.74	—	6.62	7.77	—	5.27

of 0.01 mole of sodium methylate in 15.0 ml of methanol. After 1 hour, the methanol was distilled off under reduced pressure and the residue was dissolved in water. The aqueous solution was filtered and acidified with hydrochloric acid. The diester precipitated was filtered off under suction and recrystallized. The dimethyl esters, prepared in this way, gave no mixed melting point depression with samples prepared from the corresponding arylsulfonamidophosphoric acids (Table 2).

Dipotassium salts of acid monofluorides of arylsulfonamidophosphoric acids. The trichlorophosphazosulfonaryls or acid dichlorides of the arylsulfonamidophosphoric acid, (0.01 mole) were added slowly, with stirring, to a saturated solution of 10.0 g of crystalline potassium fluoride. The reaction mixture was heated on a water bath, until the deposit had dissolved completely and then for a few minutes further, at 80-85°. The product, which came down on cooling, was filtered off under suction and recrystallized from aqueous alcohol. Yields were determined for the crystallized materials (Table 3). All the dipotassium salts obtained crystallized from aqueous alcohol in the form of platelets.

SUMMARY

By the action of trichlorophosphazosulfonaryls, or of acid dichlorides of arylsulfonamidophosphoric acids, on a saturated aqueous solution of potassium fluoride, according to the conditions of the reaction, there were obtained, successively, the potassium salts of the acid dichlorides, the potassium salts of the acid difluorides and the dipotassium salts of the acid monofluorides, of arylsulfonamidophosphoric acids. The structures of the potassium salts of the acid difluorides were confirmed by conversion of the latter to the corresponding methyl esters, by reaction with sodium methylate. It was shown that the potassium salts of the acid difluorides were even more resistant to hydrolysis than the potassium salts of the acid dichlorides, and the reason for this was discussed.

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DIPHENYLAMIDES OF TRICHLOROPHOSPHAZOCARBONIC ACIDS AND THEIR DERIVATIVES

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There is at present only one method known for preparing derivatives of the N-phosphoric acids of urea (carbamidophosphoric acids), namely the addition of primary or secondary amines to the chloroanhydrides or esters of isocyanatophosphoric acid [1]. Moreover, the product of the reaction of phosphorus pentachloride with urea is bistrichlorophosphazocarbonyl [2], which is a derivative of N,N'-carbamidobisphosphoric acid. In order to develop a general method for obtaining N,N-disubstituted carbamido-N'-phosphoric acids and their derivatives, and at the same time to extend the range of use of the reaction of phosphorus pentachloride with the amides of acids, we have investigated the reaction between phosphorus pentachloride and N,N-diphenylurea.

In carbon tetrachloride solution, at 70-80°, phosphorus pentachloride reacted almost quantitatively with N,N-diphenylurea to give the diphenylamide of trichlorophosphazocarbones acid, in accordance with the equation

$$(C_6H_5)_2NCONH_2 + PCl_5 \rightarrow 2HCl + \underset{(I)}{(C_6H_5)_2NCON{=}PCl_3}$$

The diphenylamide of trichlorophosphazocarbonic acid (I) was analogous, on the one hand, to the recently obtained trichlorophosphazoacyls [3], and, on the other hand, to the dialkylamides of trichlorophosphazosulfuric acid [4].

(I) was a low-melting crystalline material, which could only be distilled without decomposition in a high vacuum, readily hydrolyzed by water, and reacting vigorously with alcohols, phenols and amines. Under the action of anhydrous formic acid, depending on the conditions, (I) gave all the theoretically possible phosphorus-containing hydrolysis products, namely – the dichloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid $(C_6H_5)_2NCONHPOCl_2$ (II), the monochloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid

$$(C_6H_5)_2NCONHPO(OH)Cl \quad (III)$$

and free N,N-diphenylcarbamido-N'-phosphoric acid

$$(C_6H_5)_2NCONHPO(OH)_2 \quad (IV).$$

Further hydrolysis gave diphenylamine, carbon dioxide and phosphaminic acid.

(II), obtained from (I), was found to be identical with the product of addition of diphenylamine to the chloroanhydride of isocyanatophosphoric acid [1], which, together with the means of preparation and the analytical data, rigidly proved the structures (II) and (I).

(I) was hydrolyzed by the action of water vapor in CCl_4 solution to give (II), and in benzene or dioxane solution to give (III). (II), (III) and (IV) were crystalline compounds with properties recalling those of the hydrolysis products of trichlorophosphazosulfon compounds [5] and of trichlorophosphazoacyls [6], although from the latter, in spite of its resemblance to (I), it has not yet been possible to obtain hydrolysis products of type (III), i.e. monochloroanhydrides of acylamidophosphoric acids. (II) hydrolyzed with considerably more difficulty than (I), and (III) with more difficulty then (II). The reason for this has been discussed in a previous paper [7].

On reaction with sodium arylates, (I) gave satisfactory yields of the diphenylamides of the corresponding triaroxyphosphazocarbonic acids, of the type $(C_6H_5)_2NCON{=}P(OAr)_3$ (V), and these were low-melting crystalline

substances or viscous liquids of a neutral character. The chemical properties of (V) were intermediate between, on the one hand, the triaroxyphosphazosulfon-aryls [8], or -alkyls [9], and, on the other hand, the triaroxyphosphazotrichloroacetyls [10] and the triaroxyphosphazoacyls of the aromatic series [7]. The latter can only be obtained under conditions of complete exclusion of moisture; on shaking with water at room temperature, or on storage in air, they are rapidly hydrolyzed to the diesters of acylamidophosphoric acids [7]. The triaroxyphosphazotrichloroacetyls [10] hydrolyze with rather more difficulty. The diphenylamides of the triaroxyphosphazocarbonic acids (V) hydrolyzed much more easily than the triaroxyphosphazosulfoncompounds [8], but with much more difficulty than the triaroxyphosphazoacyls of the aromatic series and of the trichloracetic acid class [7, 10]. For this reason, (V) could be synthesized under normal conditions, and their solutions in nonpolar solvents could be washed with water and weak alkali (like triaroxyphosphazosulfon compounds), but they hydrolyzed easily on boiling with 96% alcohol in the absence of alkali, or on prolonged agitation of their solutions in nonpolar solvents with water at room temperature (like the triaroxyphosphazoacyls). Thus the rate of hydrolysis of triaroxyphosphazoacyls of the type $AcN=P(OAr)_3$ markedly increases along the Ac series:

$$RSO_2 < (C_6H_5)_2NCO < CCl_3CO < ArCO$$

The reason for the relative difficulty of hydrolysis of the triaroxyphosphazosulfon compounds, as compared with the triaroxyphosphazoacyls, has been previously discussed [7]. The probable explanation of the relative resistance to hydrolysis of the diphenylamides of triaroxyphosphazocarbonic acids (as compared with other triaroxyphosphazocarbacyls) is that, in the series Ac, ArCO, CCl_3CO, $(C_6H_5)_2NCO$, for the given type of compound, the $(C_6H_5)_2N$ group is the most electronegative, and therefore "interferes" most with the conjugation of the bonds $O=C$ and $N=P$, i.e. it most reduces the electrophilic character of the phosphorus atom, and therefore reduces the rate of hydrolysis.

As with all other types of triaroxyphosphazocompounds, hydrolysis of the diphenylamides of trinitrotriphenoxyphosphazocarbonic acid: (IX and X) took place much more easily (by the action of 96% ethanol at room temperature) than that of the diphenylamides of a triaroxyphosphazocarbonic acid without electronegative substituents in the aroxy groups.

Hydrolysis of the diphenylamide of a triaroxyphosphazocarbonic acid (V) affected not only the N=P linkage, but also the C-N bond so that, as well as the diester of the N,N-diphenylcarbamido-N'-phosphoric acid, 10-20% of diphenyl was always obtained. Hydrolysis of the C-N bond was complete when (V) was boiled, in aqueous alcohol solution, with 2 equiv. of caustic alkali.

The diaryl esters of N,N-diphenylcarbamido-N'-phosphoric acid were colorless crystalline substances, melting at a lower temperature than the diphenylamides of the corresponding triaroxyphosphazocarbonic acids, titrating with caustic alkali as monobasic acids in the presence of phenolphthalein, and decomposing on boiling with alkali to give diphenyl and the esters of phosphaminic acids. The remaining properties of the compounds obtained are described in the experimental part.

EXPERIMENTAL

Diphenylamide of trichlorophosphazocarbonic acid (I). A mixture of 0.01 mole of carefully dried and powdered N,N-diphenylurea, 0.01 mole of phosphorus pentachloride and 50.0 ml of CCl_4 was heated with stirring under a reflux condenser, on a water bath at 70-80°. The evolution of hydrogen chloride began immediately and the reactants gradually went into solution. All had dissolved after 30 minutes, and the evolution of hydrogen chloride slackened. The hot solution was filtered after 45 minutes, and the bulk of the solvent was distilled off, under reduced pressure, at 35-40°. The substance (I) precipitated, after cooling, in the form of fine colorless needles, which were filtered off under suction, washed with CCl_4 and dried in vacuo. The mother liquor was evaporated to a small volume and the (I) precipitated was filtered off. The total yield was about 100%, of m.p. 112-114°. The hydrogen chloride liberated in the reaction was absorbed in water and titrated. Yield about 100%. (I) was easily soluble in acetone and dioxane, with difficulty in benzene and CCl_4, and with great difficulty in ether and petroleum ether.

Found %: Cl 30.09. Equiv. after hydrolysis 5.08, 5.06. $C_{13}H_{10}ON_2PCl_3$. Calculated %: Cl 30.66 Equiv. after hydrolysis 5.00.

Dichloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid (II). a) Obtained from (I) by the action of HCOOH. A solution of 0.01 mole of (I) in 30.0 ml of benzene was treated with a solution of 0.01 mole of anhydrous HCOOH in 20.0 ml of benzene. A vigorous evolution of CO and HCl began immediately, and (II) was precipitated from the solution in the form of fine, colorless, transparent prisms. The reaction was complete after 20-30 minutes; the (II) was filtered off under suction, washed with benzene and dried in vacuo. The total yield was about 95%, m.p. 136-137° (decomp.). (II) was readily soluble in acetone, chloroform, dioxane and dichloroethane, dissolved on boiling in benzene and CCl_4, and was insoluble in ether and petroleum ether.

Found %: Cl 21.19, 21.32. Equiv. after hydrolysis 3.98, 3.98. $C_{13}H_{11}O_2N_2PCl_2$. Calculated %: Cl 21.58. Equiv. after hydrolysis 4.00

In a previous paper [11], the analytical data and melting points in the table were transposed for the dichloroanhydrides of N,N-diphenylcarbamido-N'-phosphoric acid and N,N-phenylethylcarbamido-N'-phosphoric acid. It should be noted that the m.p. of the former is 136-137° (decomp.) and of the latter 113-114° (decomp.).

b) Preparation from the chloroanhydride of isocyanatophosphoric acid and diphenylamine (Cf. [11]). A solution of 0.02 mole of diphenylamine in 10.0 ml of benzene was added slowly, with cooling (from + 5 to +10°) and stirring, to a solution of 0.02 mole of the chloroanhydride of isocyanatophosphoric acid in 10.0 ml of benzene. After 30 minutes, the crystalline precipitate formed was filtered off under suction, washed with benzene, dried in vacuo and recrystallized from CCl_4. The total yield (including recovery from the mother liquor) of about 91%, m.p. 136-137°, gave no mixed melting point depression with (II) obtained by method a).

c) Preparation from (I) by the action of water vapor. Three beakers, half filled with solutions of (I) in benzene, dioxane and CCl_4, and a fourth beaker of water, were placed in a desiccator. The surfaces of the solutions gradually became covered with crystals, and these soon filled the whole volume of liquid. They were filtered off under suction after 3 hours, and washed with the corresponding solvent. The yields were variable and not good. The product, precipitated from CCl_4, was identified as (II) by its m.p. of 132-136° and mixed melting point. The products, precipitated from benzene and dioxane, were identified as (III) by their m.p. of 171-174°, by mixed melting point and by titration.

Monochloroanhydride of N,N-diphenylcarbamido-N'-phosphoric acid (III). A solution of 0.01 mole of anhydrous HCOOH in 50.0 ml of benzene was added to a boiling solution of 0.01 mole of (II) in 50.0 ml of benzene, and the mixture was boiled under a reflux condenser for 1 hour. By then more than 100% of hydrogen chloride (absorbed in water and titrated) had been evolved. After a day, the precipitate of (III) (an aggregate of fine prisms) was filtered off under suction, washed with warm benzene and dried in vacuo. Yield 61.9%, m.p. 172-176° (decomp.). (III) was readily soluble in dioxane and chloroform, but insoluble in benzene, CCl_4, ether and petroleum ether; it was readily soluble in water and alcohol (with decomposition).

Found %: Cl 11.19; Equiv. after hydrolysis 3.08, 3.07. $C_{13}H_{12}O_3N_2PCl$. Calculated %: Cl 11.43. Equiv. after hydrolysis 3.00.

N,N-diphenylcarbamido-N'-phosphoric acid (IV). A mixture of 0.03 mole of HCOOH and 20.0 ml of benzene was added slowly, with vigorous stirring, to a solution of 0.01 mole of (I) in 50.0 ml of benzene. The reaction went vigorously at the start, but ceased after 15 minutes. The mixture was then boiled for 4 hours under a reflux condenser. By this time about 90% of the hydrogen chloride had been evolved. The precipitate formed on cooling was filtered off under suction, washed with warm benzene and dried in vacuo. Yield 63.7%. The product was a fine crystalline powder which decomposed with swelling at 110°, deliquesced in air, was readily soluble in water, but with difficulty in alcohol, was insoluble in nonpolar solvents, and did not contain chlorine.

Found %: 2.03. $C_{13}H_{13}O_4N_2P$. Calculated %: Equiv. 2.00.

Diphenylamide of triphenoxyphosphazocarbonic acid (VI). A solution of 0.02 mole of (I) in 50.0 ml of benzene was added with vigorous stirring to a suspension of 0.06 mole of dry sodium phenate in 50.0 ml of benzene. Considerable heat was evolved and the form of the suspended matter altered. The reaction mixture was boiled with stirring under a reflux condenser for 30 minutes, cooled to 0° and shaken vigorously with 50.0 ml of 0.2 N caustic soda (precooled to 0°); the benzene solution was quickly separated, washed three times with ice water and filtered through two funnels, one above the other, each containing a filter paper and 3 g of

anhydrous sodium sulfate. The more quickly these operations were carried out, the greater was the yield of VI. The benzene solution was evaporated under reduced pressure, leaving a residue, VI, in the form of a colorless transparent liquid. Yield about 90%. This nearly all crystallized after a day. The crystals were pressed, washed with petroleum ether and dried in vacuo. The product was a colorless material, of a neutral character, crystallizing in the form of fine plates, of m.p. 83-84°, readily soluble in benzene, alcohol, dichloroethane, acetone, ether and CCl_4; it dissolved in petroleum ether on heating with aqueous alcohol to give the diphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid.

Found %: N 5.16, 5.55. $C_{31}H_{25}O_4N_2P$. Calculated %: N 5.39.

Diphenylamide of tri-p-chlorotriphenoxyphosphazocarbonic acid (VII) A solution of 0.02 mole of I in 20.0 ml of benzene was added with vigorous stirring to a solution of 0.06 mole of sodium p-chlorophenate in 120 ml of ether. When the vigorous reaction had finished, the mixture was boiled under a reflux condenser, for 15 minutes. Subsequent treatment was the same as for VI. The yield was about 80%. The product crystallized in the form of fine needles of m.p. 128-130° and was readily soluble in benzene, ether, dioxane, dichloroethane, chloroform and acetone, dissolved on boiling in alcohol and CCl_4, and with difficulty in boiling petroleum ether.

Found %: N 4.41. $C_{31}H_{22}O_4N_2PCl_3$. Calculated %: 4.49.

The diphenylamide of tri-o-chlorotriphenoxyphosphazocarbonic acid (VIII) was obtained in the same way as VII. The yield was about 80%. (VIII) crystallized with great difficulty in the form of fan-shaped aggregates of needles, of m.p. 40-43°, and was readily soluble in ether and benzene, and with difficulty in CCl_4, acetone, chloroform and dichloroethane; it dissolved with difficulty in boiling petroleum ether.

Found %: N 4.51, 4.59. $C_{31}H_{22}O_4N_2PCl_3$. Calculated %: N 4.49.

Diphenylamide of tri-o-nitrotriphenoxyphosphazocarbonic acid (IX) The reaction was carried out in the same way as for (VI). Precipitated sodium chloride and a small quantity of nitrophenate were filtered off under suction and the benzene solution was boiled with active carbon the carbon was filtered off; and the benzene solution was evaporated under reduced pressure at 40°. The residue was in the form of a yellow oil (yield 83.9%). This dissolved readily in benzene, chloroform, dichloroethane, dioxane, acetone and CCl_4, but was insoluble in ether and petroleum ether. It hydrolyzed to (XV) on shaking with 96% ethanol.

Found %: N 10.81, 10.84. $C_{31}H_{22}O_{10}N_5P$. Calculated %: N 10.69.

Diphenylamide of tri-o-nitrotriphenoxyphosphazocarbonic acid (X) The reaction was carried out as for (VI), but it was necessary to boil the mixture with stirring under a reflux condenser for 8 hours. Subsequent treatment was the same as for (IX). Yield 91.4%. The product was a thick, very viscous, dark yellow oil; it was readily soluble in benzene, chloroform, dichloroethane, dioxane and acetone, and dissolved on heating in CCl_4, but was insoluble in ether and petroleum ether. It hydrolyzed to (XV) on shaking with 96% ethanol.

Found %: N 10.49, 10.70. $C_{31}H_{22}O_{10}N_5P$. Calculated %: N 10.69.

(IX) and (X) hydrolyzed considerably more easily than (VI-VIII); for this reason, treatment with aqueous solutions is not recommended in the isolation of (IX) and (X).

Diphenylamide of tri-α-naphthoxyphosphazocarbonic acid (XI). This was obtained in the same way as (VII). Yield about 70%. The product was a colorless, glass-like material, of m.p. 47-50°, readily soluble in ether, benzene, acetone, chloroform and dichloroethane, but insoluble in petroleum ether.

Found %: N 4.21. $C_{43}H_{31}O_4N_2P$. Calculated %: N 4.18.

Diphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XII) A mixture of 0.01 mole of (VI) and 50.0 ml of 96% ethanol was boiled, under a reflux condenser for 2 hours. (XII) deposited on cooling, in the form of coarse transparent prisms with truncated angles. The product was filtered off under suction, washed with alcohol and dried in vacuo. Yield 74.3%, m.p. 147-149°.

Found %: N 6.38. Equiv. 1.02. $C_{25}H_{21}O_4N_2P$. Calculated %: N 6.30. Equiv. 1.00.

Diphenylamine (13.6%) was recovered from the mother liquor and identified by mixed melting point.

Di-p-chlorodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XIII). This was obtained in the same way as (XII). The yield was 55.2%, of m.p. 151-152°, and the material crystallized from ethanol in the form of fine needles.

Found %: N 5.60. Equiv. 0.990. $C_{25}H_{19}O_4N_2PCl_2$. Calculated %: N 5.46. Equiv. 1.000.

Di-o-chlorodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XIV). This was obtained in the same way as (XII). The yield was 41.4%, of m.p. 63-65°, and the product crystallized from ethanol in the form of fine prisms.

Found %: N 5.56, 5.71. Equiv. 0.994, 0.998. $C_{25}H_{19}O_4N_2PCl_2$. Calculated %: N 5.46, Equiv. 1.000.

Substances (XII-XIV) were readily soluble in acetone and chloroform, and in boiling benzene, alcohol and CCl_4, but were insoluble in ether and petroleum ether; they could be titrated with caustic alkali as monobasic acids, in the presence of phenophthalein.

Di-p-nitrodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XV). 0.01 mole of (IX) was shaken vigorously with 50.0 ml of 96% ethanol. The oily (IX) dissolved rapidly, and, at the same time (XV) precipitated in the form of fine crystals. The product was filtered off under suction, washed with alcohol and dried in vacuo. Yield 72.1%, m.p. 148-150°.

Found %: N 10.51. Equiv. 1.004. $C_{25}H_{19}O_8N_4P$. Calculated %: N 10.49. Equiv. 1.000.

Di-o-nitrodiphenyl ester of N,N-diphenylcarbamido-N'-phosphoric acid (XVI). This was obtained in the same way as (XV). The yield was 31.8%, of m.p. 182-183°, and the product crystallized in the form of fine prisms.

Found %: N 10.55, 10.72. Equiv. 1.005, 0.980. $C_{25}H_{19}O_8N_4P$. Calculated %: N 10.49. Equiv. 1.000.

(XV) and (XVI) were readily soluble in acetone and dioxane, and in boiling alcohol, benzene, dichloroethane and chloroform, but were insoluble in ether, petroleum ether and CCl_4.

Hydrolysis of (V) with 2 equiv. of caustic alkali. A mixture of 0.005 mole of (V) with 20.0 ml of ethanol and 10.0 ml of N aqueous sodium hydroxide was boiled under a reflux condenser for 2 hours. The alcohol was distilled off under reduced pressure, whereupon the diphenyl precipitated from the aqueous solution in the form of crystals. The yield was quantitative. The product was identified by the mixed melting point method.

SUMMARY

The reaction of phosphorus pentachloride with N,N-diphenylurea has been investigated. The diphenylamide of trichlorophosphazocarbonic acid was obtained together with all its possible hydrolysis products (without degradation).

Diphenylamides of triaroxyphosphazocarbonic acids and diaryl esters of N,N-diphenylcarbamido-N'-phosphoric acids were obtained and their properties described.

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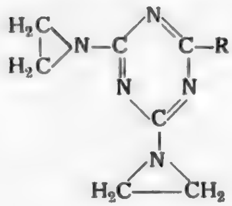
*Original Russian pagination. See C-B Translation.

triazine ring was more complicated. The replacement of chlorine by an amino-acid group in 2,4-di-(ethylene imino)-6-chloro-1,3,5-triazine, or even in cyanuric chloride, did not take place, in spite of the use of different conditions of reaction. If esters were used instead of free amino-acids, successful results were only obtained if the ester was first allowed to react with cyanuric chloride, and ethyleneimino groups were then introduced into the product.

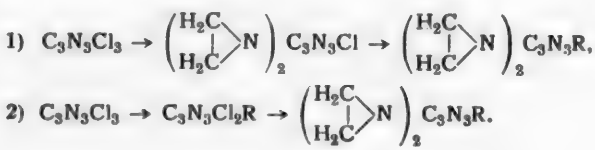
The details of the stages of the preparations varied from case to case; but it is possible to make some generalizations. The solvents used were anhydrous benzene, ether or methylene chloride. In the reaction of cyanuric chloride with amino-acid esters, the temperature conditions varied from 5-10° (exp. 5 and 6), room temperature (exp. 7, 8, 11, 13) to 30-40° (exp. 9). The reaction of 6-substituted 2,4-dichloro-1,3,5-triazines

Among 1,3,5-triazine derivatives, great interest attaches to 2,4,6-triethyleneimino-1,3,5-triazine as a possible drug for the treatment of some forms of cancer. The interesting physiological properties of this substance have attracted the attention of investigators, with the result that a large number of similar compounds have been prepared, and much new information has been obtained on the chemistry of the ethyleneiminotriazines.

In the search for improved therapeutic agents for the treatment of cancer, we undertook the synthesis of 2,4-di-(ethyleneimino)-1,3,5-triazines having as a third substituent (R) in the triazine ring either a nitrogen-containing heterocyclic radical or the groupings of the esters of aliphatic or arylaliphatic amino-acids.



To prepare the substituted 1,3,5-triazines, the starting material was usually cyanuric chloride, in which the chlorine atoms were all or partly replaced by other groups of radicals. The substituents could be introduced in various ways, depending on the nature of the reagent and the reaction conditions [1]. Two means of synthesis could be used: 1) starting from the known substance 2,4-di-(ethyleneimino)-6-chloro-1,3,5-triazine, and replacing the chlorine in it by the corresponding amino compound, or 2) starting from cyanuric chloride, replacing only one chlorine atom by the amino compound, and then allowing the substituted 2,4-triazine to react with ethyleneimine



We used both methods.

Compounds containing heterocyclic radicals (morpholyl, piperazyl and methylpiperazyl derivatives) were obtained by the first method, but 2,4-di-(ethyleneimino)-6-piperidyl-1,3,5-triazine by the second. In all cases, the reaction was carried out in an anhydrous solvent (benzene or ether) and triethylamine was used to fix the hydrogen chloride evolved. As would be expected, both the imino groups of piperazine reacted; the bis-[2,4-di-(ethyleneimino)-1,3,5-triazine-6]- piperazine formed was insoluble in water and most organic solvents, and was unsuitable for biological investigations. Attempts to obtain a singly substituted piperazine, by specially selected conditions of the reaction, were unsuccessful. The introduction of amino-acid groups into the 1,3,5-

these reagents precipitated almost quantitatively from the anhydrous solvents, and the corresponding triazine derivative remained in solution.

In the first stage it was helpful, and sometimes necessary, to seed the mixture at the beginning of the reaction with a few crystals of the hydrochloride of the corresponding amino-acid ester.

For the most part, the 6-substituted 2,4-dichloro-1,3,5-triazines were well crystallized; some of them were isolated, purified and analyzed (exp. 5,7,11), others were used for subsequent reactions without any special purification; it was also possible to dispense with their isolation and, after carrying out the reaction with cyanuric chloride, to add ethyleneimine to the solution of the substituted dichlorotriazine (exp. 8). The interaction of 6-substituted 2,4-dichloro-1,3,5-triazines with ethyleneimine took place at different speeds, depending on the structure of amino-acid; the reaction was slower the greater the molecular weight of the amino-acid. The completion of the reaction could be judged by a negative reaction of the solution for chlorine (Beilstein). The amino-acid esters required were obtained by the action of gaseous ammonia on suspensions of their hydrochlorides in ether. The yields were 80-90%. Other methods described in the literature for isolating amino-acid esters from their hydrochlorides gave too low a yield.

Since diethyleneiminotriazine derivatives containing free amino-acid groups were of special interest for biological investigations, we attempted to achieve their synthesis in another way; namely: to use compounds containing an amino-acid benzyl ester group, and to split off the benzyl group by hydrogenation. The hydrogenation of these compounds was carried out under different conditions: using xylene, ethylacetate, alcohol and other solvents, temperatures from room temperature to 90°, hydrogen pressures from atmospheric up to 60 atm., palladium, palladium on charcoal and supported nickel as catalysts. But, under the milder conditions, the starting material was recovered unchanged, and under the more drastic conditions there was isomerization of the ethyleneimine ring; this was in agreement with some data in the literature [2].

The biological activities of the compounds prepared by us will be described elsewhere, but it may be stated that (according to the results of V. A. Chernov) their general biological properties were very similar to those of triethyleneiminotriazine, but none of them showed any special features or advantages, as compared with the ethyleneimino compounds used in clinical medicine.

EXPERIMENTAL

1. 2,4-Di-(ethyleneimino)-6-morpholyl-1,3,5-triazine. A solution of 0.65 g of morpholine in 10 ml of anhydrous benzene was added, drop by drop, at room temperature, with stirring, to a solution of 1.5 g of 2,4-di-(ethyleneimino-)-6-chloro-1,3,5-triazine and 0.76 g of triethylamine in 50 ml of anhydrous benzene. Stirring was then continued for a further 1.5 hours, and the precipitated triethylamine hydrochloride (1.03 g) was filtered off; the solvent was distilled off from the filtrate under reduced pressure. The yield was 1.4 g of a substance of m.p. 121-123°. The m.p. was 135-136° after recrystallization from ethyl acetate. The product was soluble in water, alcohol, ether and benzene.

Found %: C 53.00; H 6.36; N 34.10. $C_{11}H_{16}ON_6$. Calculated %: C 53.21; H 6.47; N 33.89.

2. N-2,4-[Di-(ethyleneimino)-1,3,5-triazyl]-N'-methylpiperazine. The reaction was carried out in solution in anhydrous ether at room temperature. The reactants were 1.58 g of 2,4-di-(ethyleneimino)-6-

chloro-1,3,5-triazine in 60 ml of ether and 1.6 g of methylpiperazine in 20 ml of ether. After adding the methylpiperazine, the reaction mixture was stirred for 4 hours and then allowed to stand until the next day. After filtration, the ether was distilled off from the solution under reduced pressure, to give 1.8 g (85.4%) of a substance of m.p. 78-82°. After recrystallization from anhydrous ether, the m.p. was 82.5-83.5°. The product was soluble in water, alcohol, ether and benzene.

Found %: C 54.60; H 7.30; N 37.23. $C_{12}H_{21}N_7$. Calculated %: C 54.74; H 8.04; N 37.23.

3. N,N'-Di-[2,4-di-(ethyleneimino)-1,3,5-triazyl]-piperazine. The reaction was carried out in solution in dry methylene chloride at room temperature. The reactants were 1 g of 2,4-di-(ethyleneimino)-6-chloro-1,3,5-triazine, 0.51 g of triethylamine in 40 ml of methylene chloride and 0.21 g of piperazine in 10 ml of methylene chloride. The next day, the methylene chloride was distilled off from the reaction mixture, and the remaining colorless deposit (1.7 g) was extracted 3 times with methyl alcohol. The insoluble residue (0.9 g) gave no reaction for halogen. Yield 90.5%. The product did not melt on heating to 350°, and was insoluble in water, alcohol, ether or benzene.

Found %: C 53.12; H 5.83; N 41.39. $C_{18}H_{24}N_{12}$. Calculated %: C 52.93; H 5.92; N 41.15.

4. 2,4-Di-(ethyleneimino)-6-piperidyl-1,3,5-triazine. a) 2,4,-Dichloro-6-piperidyl-1,3,5-triazine. A solution of 2.8 g of piperidine and 3.34 g of triethylamine in 20 ml of anhydrous benzene was added to a solution of 6.1 g of cyanuric chloride in 125 ml of anhydrous benzene, the temperature of the reaction mixture being kept below 5-7°. After the addition, the reaction mixture was stirred for 3-4 hours at room temperature, and allowed to stand until the nest day. The triethylamine hydrochloride was filtered off, and the benzene was distilled off from the filtrate under reduced pressure. The remaining slightly yellow, oil was dissolved in 25 ml of ethyl acetate. The solution was filtered, and the filtrate was distilled under reduced pressure until the volume remaining was 2-3 ml. The crystals deposited were filtered off and washed with ethyl acetate. M.p. 90-91°.

Found %: Cl 30.30, 30.70. $C_8H_{10}N_4Cl_2$. Calculated %: Cl 30.42.

b). 2,4-Di-(ethyleneimino)-6-piperidyl-1,3,5-triazine. A solution of 0.37 g of ethyleneimine and 0.87 g of triethylamine in 50 ml of anhydrous benzene was added gradually, with stirring, to a solution of 1 g of 2,4-dichloro-6-piperidyl-1,3,5-triazine in 25 ml of anhydrous benzene, at 5-6°. The reaction mixture was then stirred for 4 hours at room temperature and allowed to stand until the next day. The triethylamine hydrochloride was filtered off, and the benzene was distilled off from the filtrate under reduced pressure at a temperature below 40°. The residue was dissolved in anhydrous ether. The ethereal solution was stirred up with carbon and filtered; the ether was distilled off from the filtrate under reduced pressure at room temperature. A colorless crystalline product was obtained, with a m.p. of 122° (determined by lowering a capillary into the apparatus, heated to 120°). The crystals were purified by two recrystallizations from ethyl acetate. M.p. 130.5-131.5°.

Found %: C 58.42, 58.54; H 7.32, 7.40; N 34.18, 34.22. $C_{12}H_{18}N_6$. Calculated%: C 58.51; H 7.36; N 34.12.

5. Ethyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6-]-aminoacetic acid. a) Ethyl ester of aminoacetic acid. A stream of ammonia was passed through a suspension of 5 g of the hydrochloride of aminoacetic acid ethyl ester* in anhydrous ether cooled by ice water. Ammonium chloride was filtered off, the ether was evaporated, and the residue was distilled under reduced pressure. B.p. 76.5° at 50 mm. Yield 3.36 g (91%).

The same method was used for obtaining the following amino-acid esters – methyl ester of D,L-alanine, b.p. 59° at 48 mm; ethyl ester of D,L-alanine, b.p. 58° at 45 mm; benzyl ester of D,L-alanine, b.p. 119-121° at 7 mm; methyl ester of β-aminopropionic acid, b.p. 69° at 58 mm; ethyl ester of D,L-α-aminoisovaleric acid, b.p. 91.5° at 38 mm; diethyl ester of D,L-aspartic acid, b.p. 136-137° at 15 mm; diethyl ester of D,L-glutamic acid, b.p. 126-128° at 7 mm.

b) Ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-aminoacetic acid. A solution of 2.38 g of the ethyl ester of glycine and 2.34 g of triethylamine in 20 ml of anhydrous benzene was added, drop by drop, with stirring, to a solution of 4.26 g of cyanuric chloride in 100 ml of anhydrous benzene, at 6-8°. The subsequent procedure was as in 4. After the benzene had been distilled off, the residual oil was dissolved in dry ether, and the solution was treated with carbon and filtered. The ether was distilled off, leaving 3.66 g of colorless crystals,

*Prepared by Fischer's method [3].

which were washed with petroleum ether and recrystallized from anhydrous ether. M.p. 88-89°.

Found %: C 33.45; H 3.14; N 22.66. $C_7H_8N_4O_2Cl_2$. Calculated %: C 33.48; H 3.21; N 22.32.

c) A solution of 0.86 g of ethyleneimine and 2.02 g of triethylamine in 10 ml of anhydrous benzene was added to a solution of 2.51 g of the above described compound, of m.p. 88-89°, in 75 ml of anhydrous benzene, at 10°. The mixture was then stirred for 2 hours. The solution was allowed to stand overnight and filtered; the benzene was distilled off, and the residue was dissolved in dry ethyl acetate and treated with charcoal. Filtration and evaporation of the ethyl acetate left a colorless oil, which crystallized on standing. Recrystallization from ether yielded 1.5 g of material, of m.p. 69-70°. This ethyl ester of N-(diethyleneiminotriazyl)-aminoacetic acid was readily soluble in water, alcohol, ether and ethyl acetate.

Found %: C 50.12; H 6.01; N 32.11. $C_{11}H_{16}O_2N_6$. Calculated %. C 49.99; H 6.10; N 31.80.

6. Methyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6]-D,L-α-aminopropionic acid. a) The initial methyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-α-aminopropionic acid was prepared in the same way as the derivative of the ethyl ester of aminoacetic acid (see previous experiment). Colorless crystals were obtained of m.p. 91-94°.

b) The interaction of the above starting material, of m.p. 91-94°, with ethyleneimine was carried out in solution in anhydrous ether at 5° in the presence of triethylamine. After the mixture had stood overnight, it was treated as under 5,c. The oily product was triturated with anhydrous ether to give crystals of m.p. 89-90°. These were dissolved in ethyl acetate and treated with carbon, and the solvent was distilled off to give the methyl ester of N-(diethyleneiminotriazyl)-α-aminopropionic acid, of m.p. 94-95°. This was soluble in water, alcohol, ether, benzene and ethyl acetate.

Found %: C 50.20; H 6.17; N 32.07. $C_{12}H_{18}O_2N_6$. Calculated %: C 50.00; H 6.10; N 31.80.

7. Diethyl ester of N-[2,4-di-(ethyleneimino)-1,3,5-triazyl-6]-D,L-aspartic acid. a) The diethyl ester of N-(2,4-dichoro-1,3,5-triazyl-6)-aspartic acid was obtained by adding a solution of 6.17 g of the ethyl ester of aspartic acid in 30 ml of anhydrous ether, drop by drop with stirring at room temperature, to a solution of 3 g of cyanuric chloride in 100 ml of anhydrous ether. After 1 hour, the precipitate of the hydrochloride of aspartic acid ethyl ester was filtered off, and the ether was distilled off from the filtrate. The yield was 4.77 g of the diethyl ester. M.p. 63-64°.

Found %: N 16.73. $C_{11}H_{14}O_4N_4Cl_2$. Calculated %: N 16.62.

b) A solution of 2.1 g of ethyleneimine was added, drop by drop with stirring, to a solution of 4 g of the diethyl ester of N-(dichloro-1,3,5-triazyl)-aspartic acid in 100 ml of anhydrous ether. Stirring was then continued for 2 hours. The next day, the reaction mixture was treated with charcoal and filtered, and the filtrate was concentrated to a small volume. Colorless crystals deposited after long standing. Yield 3.1 g. The m.p. was 76.5-77.5° after the product had been crystallized from anhydrous ether. The diethyl ester of N-(diethylenel-iminotriazyl)-aspartic acid was soluble with difficulty in water, and soluble in alcohol, ether, benzene and ethyl acetate.

Found %: N 23.85. $C_{15}H_{22}O_4N_6$. Calculated %: N 24.00

8. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L-α-aminopropionic acid. This was obtained in the same way as the compound described in exp. 7, with the difference that the intermediate – the ester of N-(2,4-dichloro-1,3,5-triazyl-6)-α-aminopropionic acid – was not isolated, but the ethereal solution, containing this substance, was treated with an ethereal solution of ethyleneimine. The corresponding treatment and removal of ether by distillation yielded an oil, which crystallized on standing. M.p. 95-97°. The sample for analysis was recrystallized from anhydrous ether, and melted at 100-101°. The product was soluble in water, alcohol and ether.

Found %: C 51.54; H 6.47; N 30.56. $C_{12}H_{18}O_2N_6$. Calculated %: C 51.77; H 6.55; N 30.20.

9. Benzyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L- α-aminopropionic acid. The reaction of cyanuric chloride with the benzyl ester of D,L-alanine was carried out in solution in anhydrous benzene; the temperature was maintained at 30° during the time of the reaction. After the solution had been filtered and the benzene distilled off, the ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-alanine had a m.p. of 125-126°.

The reaction of this substance with ethyleneimine was carried out in anhydrous benzene solution, with cooling. After the solution had been filtered and the benzene distilled off, the residual oil was dissolved in anhydrous ether, and the solution was treated with carbon and the ether distilled off. The colorless crystals remaining had a m.p. of 86-87°. Recrystallization from anhydrous ether gave a product of m.p. 90-91°. The product was insoluble in water, soluble in alcohol, ether and benzene.

Found %: C 59.80; H 5.80. $C_{17}H_{20}O_2N_6$. Calculated %: C 59.98; H 5.92; N 24.7.

10. Methyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-β-aminopropionic acid. The methyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-β-aminopropionic acid was prepared as described above for the other compounds of this class. The reaction was carried out in anhydrous benzene solution. Colorless crystals were obtained with a m.p. 102-103°. The reaction of this substance with ethyleneimine was performed in anhydrous ether solution. After the reaction mixture had been filtered and the solvent had been distilled off, a crystalline product was obtained, which, after recrystallization from ethyl acetate, melted at 95-96°; this was soluble in water, alcohol, ether and benzene.

Found %: C 50.15; H 6.09. $C_{11}H_{16}O_2N_6$. Calculated %: C 50.00; H 6.10.

11. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-β-phenylaminopropionic acid. a) The ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-β-phenylaminopropionic acid was prepared as described above. The reaction was carried out in anhydrous benzene solution, at room temperature. The crystalline product was recrystallized from anhydrous ether, and then melted at 110-111°.

Found %: C 48.98; H 9.33; N 16.82. $C_{14}H_{14}O_2N_4Cl_2$. Calculated %: C 49.27; H 4.11; N 16.42.

b) The reaction of ethyleneimine with the dichlorotriazine derivative was carried out in anhydrous ether solution, at 8-10°. Filtration, treatment with charcoal, and removal of solvent by distillation yielded an oil, which was treated with a fresh portion of anhydrous ether. On standing, the oil was converted into a colorless amorphous substance, which had no characteristic melting point, since it decomposed on heating.

Found %: C 60.55; H 6.43; N 23.57. $C_{18}H_{22}O_2N_6$. Calculated %: C 60.91; H 6.25; N 23.71.

12. Ethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L-α-aminoisovaleric acid. a) The ethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-α-aminoisovaleric acid was prepared from cyanuric chloride and the ethyl ester of aminoisovaleric acid. The reaction was carried out in anhydrous ether at room temperature. After the usual treatment, the oil obtained was redistilled at 0.1 mm. The oil did not solidify.

Found %: C 40.93; H 4.89; N 19.29. $C_{10}H_{14}O_2N_4Cl_2$. Calculated %: C 40.97; H 4.82; N 19.11.

b) The reaction of ethyleneimine with the dichlorotriazine derivative was carried out in anhydrous ether at 8-10°. The reaction mixture was filtered and treated with carbon, and solvent was distilled off until the residual volume was small. Colorless crystals were formed after long standing. These were recrystallized from anhydrous ether to give a product of m.p. 78-79°. This was readily soluble in ether and benzene, with difficulty in water.

Found %: C 55.02; H 7.19. $C_{14}H_{22}O_2N_6$. Calculated %: C 54.88; H 7.24.

13. Diethyl ester of N-(2,4-diethyleneimino-1,3,5-triazyl-6)-D,L-glutamic acid. The diethyl ester of N-(2,4-dichloro-1,3,5-triazyl-6)-D,L-glutamic acid was prepared as described above, the reaction being carried out in anhydrous benzene at room temperature. It was a colorless oil of b.p. 159° at 0.08 mm. The reaction with ethyleneimine was carried out in anhydrous ether. The product was a colorless transparent oil.

Found %: C 52.64; H 6.67; N 23.08. $C_{16}H_{24}O_4N_6$. Calculated %: C 52.73; H 6.64; N 23.06

SUMMARY

Some 6-substituted 2,4-di-(ethyleneimino)-1,3,5-triazines have been prepared. The substituents were nitrogen containing heterocyclic groups and aliphatic and arylaliphatic amino-acids.

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SYNTHESIS OF p-NITROPHENYLHALOGENOMETHYL CARBINOLS

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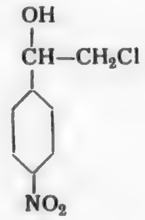
p-Nitrophenylhalogenomethyl carbinols are intermediates for the production of the synthetic antibiotic syntomycin, p-nitrophenylchloromethyl carbinol (I).



(I)

was first synthesized from styrene by V. A. Mikhalev and his co-workers[1]. Styrene chlorohydrin was acetylated, the acetyl derivative was nitrated, and the p-isomer was separated from the mixture of nitro compounds and hydrolyzed to (I).

It appeared of interest to examine the possibility of the direct nitration of styrene chlorohydrin. We found that if the sytrene chlorohydrin was added to the nitration mixture at a temperature below 0°, the product was a mixture of the nitrates of m- and p-nitrophenylchloromethyl carbinols [2]. We were able to separate the ester of the p-nitro derivative by crystallization. To establish its structure, it was oxidized with permanganate to p-nitrobenzoic acid, and it was also prepared from p-nitrophenylchloromethyl carbinol, synthesized by Mikhalev's method. The m-isomer was also isolated, and its structure was established in the same way.

It was necessary to hydrolyze the nitrate in order to obtain p-nitrophenylchloromethyl carbinol. It was found, however, that there is no method given in the literature for hydrolyzing the nitrates of alcohols without also forming considerable quantities of secondary products. In our attempts to hydrolyze the nitrate with aqueous or alcoholic alkali, we obtained much reddish tar and little carbinol. Hydrolysis did not occur when the nitrate was boiled with water and dilute acid. Smooth hydrolysis to the carbinol (with a yield of about 90%) was only achieved by heating the nitrate with a very large excess of concentrated hydrochloric acid. It was found later that it was advantageous to use a mixture of hydrochloric and phosphorous acid, since complete hydrolysis was then achieved with a smaller quantity of acid. It is interesting to note that aqueous phosphorous acid, without hydrochloric acid, did not hydrolyze the nitrate to the carbinol.

Another method of hydrolysis was also found. It is known that alkyl nitrates will nitrate aromatic compounds in the presence of aluminum chloride. It was of interest to investigate the possibility of using this process for hydrolyzing the nitrate. It was found that the nitrate of p-nitrophenylchloromethyl carbinol, on heating with benzene and aluminum chloride, gave an 85% yield of the carbinol with the simultaneous formation of nitrobenzene.

The best yield of carbinol (up to 95%) was obtained by heating the nitrate with 60-65% sulfuric acid in the presence of urea. A more dilute acid gave incomplete hydrolysis.

The nitrate of p-nitrophenylbromomethyl carbinol was obtained by Ernest and Vesely by nitrating styrene dibromide [3]; but these authors did not succeed in hydrolyzing the nitrate. We found that this nitrate could be

hydrolyzed by heating with concentrated hydrochloric acid, or preferably with 60% sulfuric acid and urea in precisely the same way as the chloromethyl derivative. p-Nitrophenylchloromethylcarbinol and p-nitrophenylbromomethyl carbinol were oxidized by sodium dichromate, in the normal way, to the corresponding p-nitrochloroacetophenone, of m.p. 91° [4], and p-nitrobromoacetophenone, of m.p. 96-97° [5].

EXPERIMENTAL

Nitrate of p-nitrophenylchloromethylcarbinol. A mixture of 153 ml of nitric acid (d 1.5) and 306 ml of concentrated sulfuric acid was kept at −2°, and 156.5 g (1 mole) of styrene chlorohydrin was added from a dropping funnel, with vigorous stirring, over a period of 3 hours. The mixture was then stirred for 1 hour at 0°. The product was poured on to ice, filtered off under suction, washed with cold water and with 40 ml of methyl alcohol, and recrystallized from methyl alcohol. Yield 90.6 g (45%). M.p. 78-80°, and 82° after a second recrystallization. The product was readily soluble in benzene, dichloroethane and acetone.

Found %: N 11.16, 11.32. $C_8H_7O_5N_2Cl$. Calculated %: N 11.35.

The mother liquor from the recrystallization was freed from solvent by distillation, and the residue was allowed to stand for two weeks. The nitrate of m-nitrophenylchloromethyl carbinol crystallized out. After two recrystallizations, this had a m.p. of 84° and gave a large m.p. depression when mixed with the nitrate of the p-compound. The m-isomer was readily soluble in dichloroethane, benzene, chloroform and acetone.

Found %: N 11.11, 11.24. $C_8H_7O_5N_2Cl$. Calculated %: N 11.35.

p-Nitrophenylchloromethyl carbinol. a) A mixture of 61.6 g of the nitrate of p-nitrophenylchloromethyl carbinol and 616 ml of concentrated hydrochloric acid was stirred vigorously and heated for 3 hours on a water bath, cooled and filtered. Yield of p-nitrophenylchloromethyl carbinol 45.4 g (90%). M.p. 78-80°.

b) The nitrate (370 g = 1.5 mole) was added gradually to a mixture of 360 g of phosphorous acid, 160 g of concentrated hydrochloric acid and 60 ml of water, and the whole was heated and stirred on a boiling water bath, for 2 hours. Without stopping the stirring, 400 ml of water was added, the mixture was cooled, and the p-nitrophenylchloromethyl carbinol was filtered off. Yield 230 g (92.5%). M.P. 78-79°.

c) Anhydrous aluminum chloride (48 g = 0.36 mole) was added, a little at a time, with stirring, to 197 g (0.8 mole) of the nitrate and 480 ml of dry benzene, at +5°. The mixture was heated slowly on a water bath and boiled for 40 minutes. Then 120 ml of water was added, and the benzene and nitrobenzene formed were distilled off in steam, separated from water and redistilled. The yield of nitrobenzene was 83.8 g (85%). The residue in the reactor was cooled with stirring and the product was filtered off, washed with dilute hydrochloric acid, carefully pressed and stirred with a mixture of 35 ml of petroleum ether and 15 ml of chloroform. The yield of p-nitrophenylchloromethyl carbinol was 137 g (85%). M.p. 78-80°.

d) A mixture of 246.5 g (1 mole) of the nitrate, 60 g (1 mole) of urea and 300 ml of 63% sulfuric acid was heated on a boiling water bath, with stirring, for 2 hours, and then diluted with 500 ml of water and cooled at 10°. The product was filtered off and washed free of acid. Yield 193 g (95%). M.p. 79-81°.

Nitrate of p-nitrophenylbromomethylcarbinol. A mixture of 27 ml of nitric acid (d 1.5) and 60 ml of concentrated sulfuric acid was cooled to −5°, and 25 g of styrene bromohydrin [6] was added, with stirring, over a period of 2 hours, after which stirring was continued for another hour at 0°. The product was poured on to ice, and the solid was filtered off, washed with water and recrystallized from ethyl alcohol. Yield 18.1 g (50%). M.p. 97-98°.

Found %: N 9.46, 9.39. $C_8H_7O_5N_2Br$. Calculated %: N 9.62.

p-Nitrophenylbromomethyl carbinol, of m.p. 84-85° [7], was easily obtained from the nitrate by the method described above: a) by hydrolysis with concentrated hydrochloric acid, in 88% yield, or b) by hydrolysis with 60% sulfuric acid and urea, in 96% yield.

SUMMARY

A method has been developed for obtaining p-nitrophenylchloromethyl carbinol and p-nitrophenylbromomethyl carbinol by nitration of the corresponding styrene halogenohydrins, and subsequent hydrolysis of the resulting nitrates.

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ABSORPTION SPECTRA AND STRUCTURE OF THE BISULFITE COMPOUND OF ACRIDINE

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The data in the literature on the structure of the bisulfite compound of acridine is contradictory. Graebe [1] first described two products of the interaction of acridine with sulfurous acid and with sodium bisulfite. One of these, $C_{13}H_9NSO_3HNa$, consisted of colorless crystals readily soluble in water; the other was red, a difficultly soluble substance, of composition $C_{13}H_{10}NSO_3H\ C_{13}H_9N$. Wirth and Lemstedt [2] later assigned to the colorless substance the structure of the sodium salt of dihydroacridine-9-sulfonic acid (I). Drozdov and Cherntsov [3] believed it to be sodium acridinium sulfite (II).

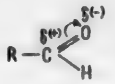
(I) (II)

Grigorovskii [4] considered that there was no real evidence for either of these structures.

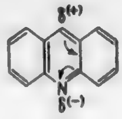
To answer the question of which of these two formulas, (I) or (II), represents the structure of the colorless bisulfite compound of acridine, we compared the absorption spectrum of this substance with those of acridine derivatives having a quinoid configuration of the pyridine ring, such as dihydroacridine and 10-methyl-9-imino acridine, or, for contrast, of the acridinium ion.

The colorless bisulfite compound of acridine was prepared by the method given in the literature [3]. The absorption spectrum was investigated at concentrations from 10^{-3} to 10^{-4} M in 0.1 N sodium sulfite solution, and at concentrations from 10^{-3} to 10^{-5} M in water and in ethanol. In the bisulfite and alcohol solutions, an absorption band was observed with a maximum at about 2770 A (Fig. 1, curves 1 and 2). There is a band in this position in the absorption spectra of dihydroacridine [5], p-anthraquinone [6] and 10 methyl-9-iminoacridine [7] (Fig. 1 curves 3-5), all of which are known to have a quinoid structure for the middle ring of the condensed system. This band in the spectrum of the bisulfite compound of acridine was conditionally called the "quinoid" band. Its appearance in the spectrum of this substance could be explained by the addition of a hydrogen atom to the nitrogen in the ring, and of the NaS_2 residue to the carbon atom in the 9 position (I). If the NaS_2 residue was attached to the 10 position of the acridinium nucleus (II), the absorption curve should resemble that of an acridine salt involving the ring nitrogen; this was not observed in practice (cf. curve 1 of Fig. 1 and curve 1 of Fig. 2).

A similar addition of sodium bisulfite has been noted for other heterocyclic compounds, such as the sulfanilamide derivatives of triazole [8]. A similar addition of sodium bisulfite is well known with compounds containing a carbonyl group. In the present case (acridine) the role of the carbonyl oxygen is fulfilled by the ring nitrogen, which is able to take up an electron. As the result of a shift of electrons in the ring in the direction of the nitrogen, the 9 carbon atom acquires a partial positive charge, and the ring nitrogen a partial negative charge. In this way there is a resemblance between the polarized acridine molecule (IV) and an aldehyde (III)



(III)



(IV)

The bisulfite compound of acridine is relatively unstable. For example, even 2 hours after the preparation of solutions in ethanol or water, in addition to the bands characteristic of the quinoid structure (I), other

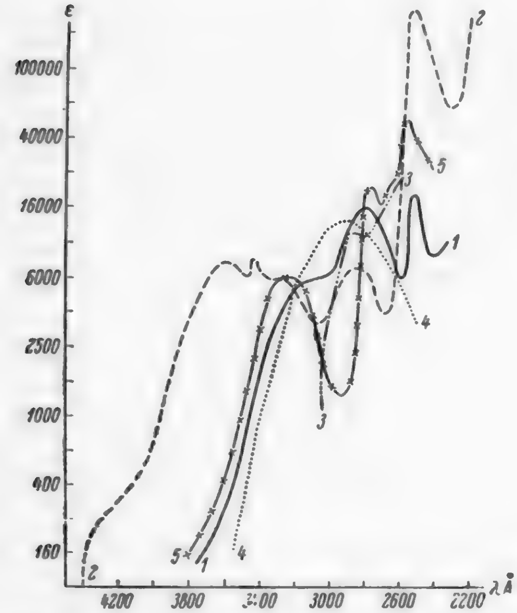


Fig. 1. Absorption spectra. 1) Bisulfite compound of acridine in 0.1 N Na_2SO_3, 2) bisulfite compound of acridine in ethanol (immediately after preparation of solution), 3) 10-methyl-9-iminoacridine [7] in methanol (part of curve), 4) dihydroacridine [5] in ethanol, 5) anthraquinone [6] in ethanol.

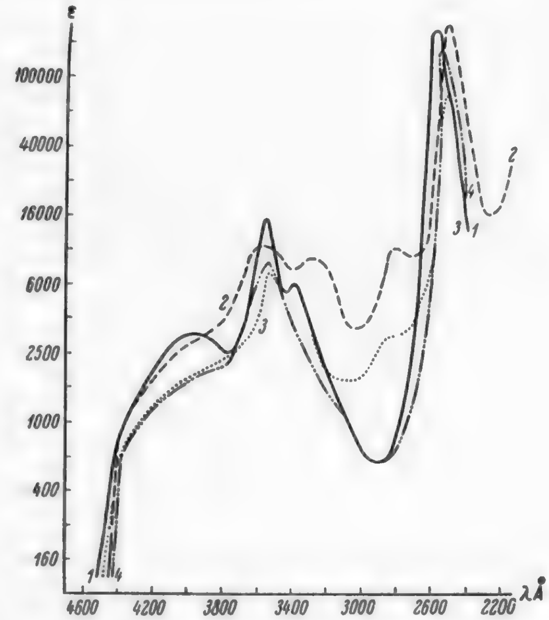


Fig. 2. Absorption spectra. 1) Acridine in a 5 M solution of HCl in ethanol, 2) bisulfite compound of acridine in water (immediately after preparation of solution), 3) bisulfite compound of acridine in water (after solution had stood for 2 hours), 4) bisulfite compound of acridine in water (after solution had stood for 6 days).

bands appeared close to those characteristic of the acridinium ion (II). The composite nature of the spectrum of the bisulfite compound could be seen by superimposing the curves (Fig. 1, curve 2 and Fig. 2, curves 2 and 3). This indicated that there was an equilibrium between the sodium salt of dihydroacridine-9-sulfonic acid (I) and the acridinium sulfite (II).

$$(I) \underset{Na_2SO_3}{\overset{H_2O}{\rightleftarrows}} (II)$$

With time (after the solution had stood for 6 days), this equilibrium was almost completely displaced towards the side of the acridinium salt (Fig. 2, curve 4, cf. curve 1). The shift of equilibrium towards increase in the acridinium salt was accompanied by a change in the color of the solution; it changed from colorless to yellow, which was brought about by the formation of a positive charge on the ring nitrogen. The reverse process – the change from a colored to a colorless solution – was produced by the addition of sodium sulfite.

SUMMARY

1. It was established that the absorption spectra of solutions of the bisulfite compound of acridine in sodium sulfite solution, and in solutions in ethanol and water immediately after preparation, had a "quinoid" absorption band. The "quinoid" band of the aqueous solution disappeared after 6 days, and there was a reversion to the spectrum of the acridinium ion.

2. The colorless bisulfite compound of acridine, $C_{13}H_{10}O_3NSNa \cdot 2H_2O$, has been shown to have the structure of the sodium salt of dihydroacridine-9-sulfonic acid, and to change, under the influence of water, to a sulfite (with participation of the ring nitrogen).

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ABSORPTION SPECTRA AND STRUCTUREOF 2-METHOXY-AMINOACRIDINE-9

V. I. Blizniukov and A. K. Sukhomlinov

The spectrographic investigation of 2-methoxy-9-aminoacridine is of interest because acridine, with a methoxy group in the 2 position, has considerable anti-malarial activity [1]. We have studied the absorption spectra of 2-methoxy-9-aminoacridine in solution in ethanol, dioxane, ether, a M solution of sodium ethylate, ethanol solutions of hydrogen chloride of different concentrations, and in concentrated sulfuric acid, at concentrations from 10^{-3} to 10^{-5} M.

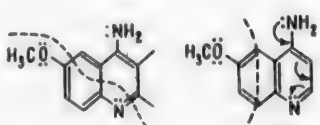
Analysis of the absorption spectra in neutral solvents (Fig. 1, compare curves 1, 2, 5 and 6 with 3 and 4) showed that the "benzenepyridinic"spectrum of acridine was preserved with a 2-methoxy group and a 9-amino group in the acridine ring system. Two absorption bands were observed in these spectra – one, with a maximum at λ 3500 A (ϵ = 1800), is also present in the spectrum of anthracene, and was therefore called "anthracenic", the other, observed as a shoulder at λ 2950 A* (ϵ = 6000), is characteristic of a para disubstituted benzene in which both the substituents are electron donors [3] (such as p-anisidine), and therefore called "p-anisidinic".

The introduction of a methoxy group into the 2 position of the 9-aminoacridine ring system also resulted in a displacement of the benzenoid bands in the direction of longer wave length, and in the development of a fine structure in the "pyridinic" and long-wave benzenoid bands, of 2-methoxy-9-aminoacridine (Fig. 1, compare curves 1 and 3).

With the solutions in ether and sodium ethylate solution, a "p-aminopyridinic" band was observed with a maximum at λ 2600 A (Fig. 1, curves 5 and 6). The anthracenic band, of λ_{max} 3500 A (without the pyridinic band), was also apparent in the spectrum of 9-aminoacridine, when both the ring nitrogen and the amino group had formed salts (Fig. 1, part curve 7). Two other 2-methoxy-9-aminoacridine bands, with maxima at about λ 3350 and 3200 A, were observed in the spectrum of the diacid salt of 9-aminoacridine, and must therefore not be considered as anthracenic bands, but as due to the fine structure of the pyridinic band.

The appearance of two benzenoid bands of the para type in the spectrum of 2-methoxy-9-aminoacridine can be explained as due to the interaction of groups through the π-electrons of the acridine ring system.

The band with a maximum at λ 2950 A (ϵ = 6000) is due to electron interaction between the ring nitrogen and the methoxybenzene ring and the methoxy group (I).



(I) (II)

A similar interaction of ring nitrogen with a benzene ring and a methoxy group has been previously demonstrated by one of us for a number of quinoline derivatives [2].

* The mean point of the curve was taken.

The appearance, in the 2-methoxy-9-aminoacridine spectrum, of an absorption band with a maximum at λ 2600 A is explained by a coupling of the ring nitrogen (electron attracting) with the amino group, through the π-electrons of the pyridine ring (II). The same effect was shown previously for 4-aminopyridine and 4-aminoquinoline [2,4].

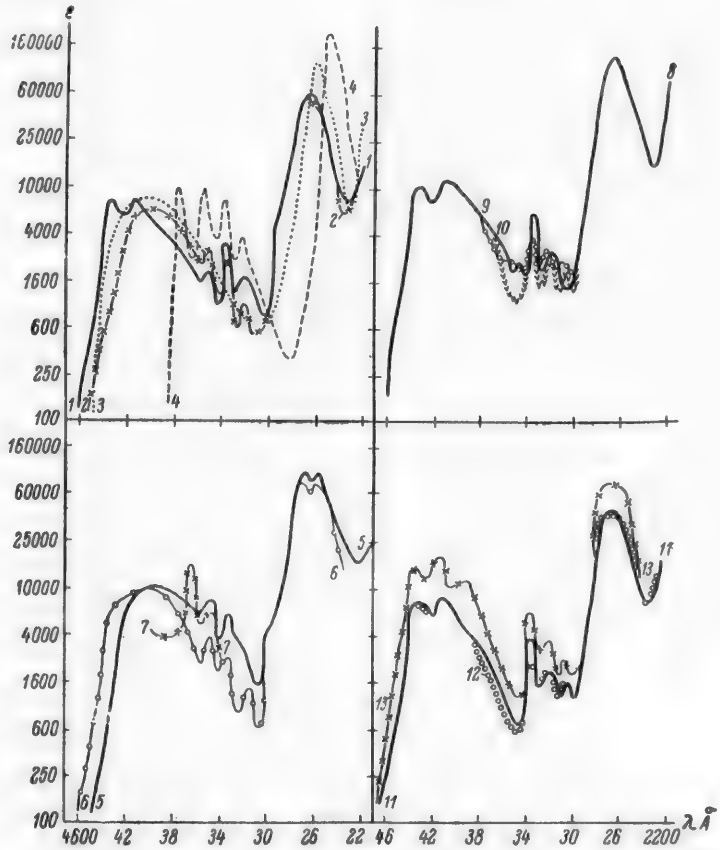


Fig. 1. Absorption spectra. 1) 2-Methoxy-9-aminoacridine in ethanol, 2) 2-methoxy-9-aminoacridine in dioxane, 3) 9-aminoacridine in ethanol, 4) anthracene in hexane, 5) 2-methoxy-9-aminoacridine in ether, 6) 2-methoxy-9-aminoacridine in M sodium ethylate, 7) 9-aminoacridine in 17.5 M H_2SO_4 (part of curve), 8) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1 : 0.2 mole HCl), 9) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1 : 0.3 mole HCl), 10) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1 : 0.5 mole HCl), 11) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1 : 1 mole HCl), 12) 2-methoxy-9-aminoacridine in ethanolic HCl (ratio 1 : 100 mole HCl), 13) 2-methoxy-9-aminoacridine in 5 M ethanolic HCl.

In acid ethanolic solutions of hydrogen chloride, even at a ratio of 1 : 0.4 mole HCl, the anthracenic band at λ 3500 A and the p-anisidinic shoulder at λ 2950 A were not apparent. The fine structure of the pyridinic band was also better developed, with three maxima at λ 3350, 3320 and 3050 A (Fig. 1, curves 10-13). The same shown for "quinoline-45" [2]. At a ratioof 0.3 mole HCl to 1 mole of 2-methoxy-9-aminoacridine, the third maximum of the fine structure of the pyridinic band appeared at λ 3080 A, and the anthracenic band at λ 3550 A had disappeared, (Fig. 1, curve 9).

Thus in neutral solution, the separate interactions of the ring nitrogen, both with the π-electrons of the methoxybenzene ring and the methoxy group, and with the π-electrons of the pyridine ring and the amino group, lead to favorable conditions for electron transfer, in which the ring nitrogen can either attract or give up an electron. In acid media, because the ring nitrogen acquires a positive charge, there is an increase in its capacity to attract an electron from the amino group via the π-electrons of the pyridine ring. This is why the p-anisidinic and anthracenic bands, with maxima at λ 2950 and 3500 A, disappeared from the spectrum of 2-methoxy-9-aminoacridine in acid solution.

The electron interaction of the ring nitrogen with the methoxy and amino groups is confirmed by the dipole moments of 2-methoxy-9-chloroacridine and of 9-aminoacridine. According to Z. Iu. Kokoshko [5], the dipole moment of 2-methoxy-9-chloroacridine is 0.47 D greater than the moment of the linkage of the methoxy group to the ring: $\mu_{exp} = 1.70$ D, $\mu_{calc} = 1.23$ D. For 9-aminoacridine the dipole moment is 0.85 D greater than that calculated from the amino group: $\mu_{exp} = 4.13$ D, $\mu_{calc} = 3.28$ D.

The formation of a diacid salt of the 9-amino group and the ring nitrogen of 2-methoxy-9-aminoacridine in concentrated sulfuric acid (Fig. 2, curve 1) eliminated the effect of the amino group on the acridine system. Salt formation by the methoxy group did not occur, since there was no reversion to the spectrum of unsubstituted acridine in concentrated sulfuric acid. The effect of the methoxy group in the 2 position was shown only by the bathochromic shift of the absorption bands (Fig. 2, curves 1 and 2).

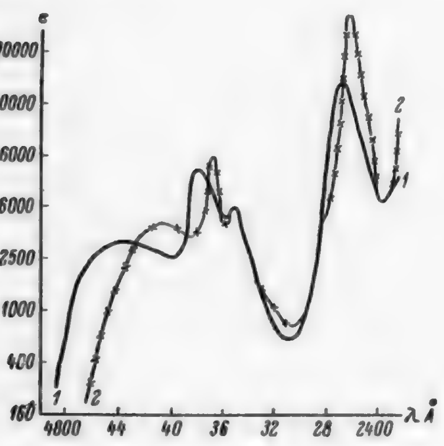


Fig. 2. Absorption spectra. 1) 2-Methoxy-9-aminoacridine in 17.5 M. H_2SO_4, 2) 9-aminoacridine in 17.5 M H_2SO_4.

SUMMARY

1. The effect of solvent and of the acidity of the solution on the absorption spectrum of 2-methoxy-9-aminoacridine has been investigated, and it has been shown that the ring nitrogen can attract or give up an electron under the influence of the substituent group.

2. The complicated spectrum of 2-methoxy-9-aminoacridine has been interpreted as "benzene-pyridinic", on which are superimposed three bands corresponding to the separate interactions of the substituent groups with the ring nitrogen, through the π-electrons of the acridine ring system.

3. It has been established that 2-methoxy-9-aminoacridine forms a diacid salt in concentrated sulfuric acid, involving both the ring nitrogen and the amino group.

In conclusion, we would offer our deepest thanks to A. M. Grigorovskii for his kind gift of 2-methoxy-9-aminoacridine for the spectrographic investigation.

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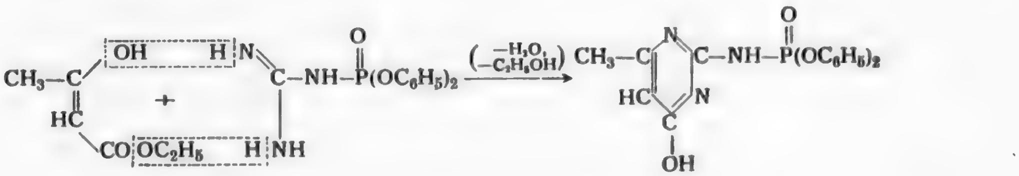
SYNTHESIS OF PHOSPHORAMIDOPYRIMIDINES

Iu. P. Shvachkin and M. A. Prokof'ev

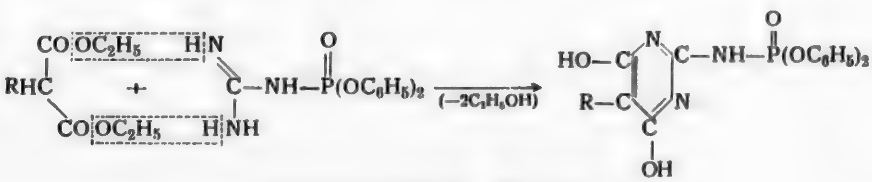
Chemical literature lacks data on phosphorylated aminopyridines. At the same time a study of compounds of this type is of undoubted interest both from theoretical considerations (for example, in connection with the problem of the character of internucleotidic bonds in macromolecules of nucleic acids) and from the practical point of view. Specifically, it is reasonable to expect that the phosphorylated aminopyrimidines may turn out to be analogous in biological activity to the phosphorylated hydroxypyrimidines, among which in recent times some valuable insecticides have been found which act effectively on insects, but which are only weakly toxic to the warmblooded animals [1, 2].

One of the possible paths of synthesis of phosphorylated 2-aminopyrimidines may be the condensation of guanidinophosphoric acids with β-dicarbonyl compounds. In the present paper there are described the syntheses of some 2-phosphoramidopyrimidines, based on the condensation of the diphenyl ester of guanidinophosphoric acid (diphenyl phosphorylguanidine) with compounds of the type of acetoacetic and malonic esters.

Acetoacetic ester condenses with diphenyl phosphorylguanidine on being heated in alcoholic solution in the presence of sodium ethoxide, forming thereby 2-diphenylphosphorylamido-4-hydroxy-6-methylpyrimidine (I) according to the scheme:

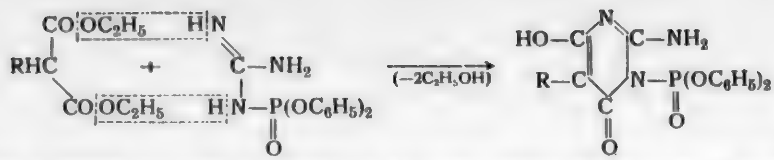


Malonic ester and its homologs condense with diphenyl phosphorylguanidine in analogous circumstances, yielding the corresponding 2-diphenylphosphorylamido-4,6-dihydroxypyrimidines:



(II) R=H, (III) R=CH_3, (IV) R=C_2H_5.

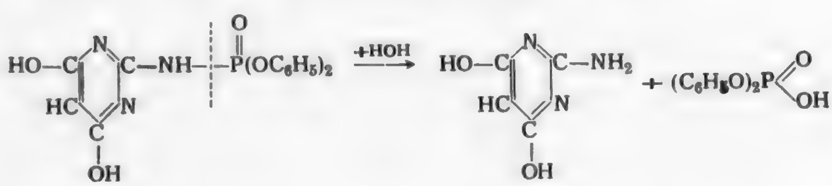
Other directions of condensation, which should lead to the isomeric 2-aminopyrimidines phosphorylated at the nuclear nitrogen, are also theoretically possible, as for example:



However such structures are rather improbable for the compounds prepared by us, since in these synthesized substances the amino nitrogen (by Van Slyke method) is totally lacking, while in the known 2-aminopyrimidines substituted at the nuclear nitrogen the amino group is detectable by this method.

The compounds prepared by us are colorless crystalline substances with rather high melting points. They are readily soluble in the lower alcohols, difficultly soluble in water and aromatic hydrocarbons, and are insoluble in diethyl and petroleum ethers, as well as in acids. In reaction with alkalis (in the cold) they pass into solution readily, binding quantitatively one equivalent of the base. Evidently this is explained by the presence in these compounds of hydroxyl groups which possess acidic properties, similar to those of the phenolic hydroxyl.

A study of the stability to hydrolysis of 4-hydroxy and 4,6-dihydroxyphosphoramidopyrimidines, performed by us with the specimens of compounds (I) and (II), showed that the phosphoramidic bond in these substances is relatively weakly stable, especially in the 4,6-dihydroxy derivatives. Thus, compound (II) is cleaved according to the following scheme in acidic, alkaline and even aqueous hydrolyses:



In this event the resulting 2-amino-4,6-dihydroxypyrimidine decomposes further, as should be expected [3, 4], into malonic acid and guanidine. In cases of acidic and basic hydrolyses there is observed the cleavage of diphenyl hydrogen phosphate which is also not unexpected [5]. In compound (I) the phosphoramidic link is more stable and is not cleaved on boiling the substance with water for one hour. Heating of the compound with normal base or acid leads to a slow cleavage of the phosphoramidic link according to the scheme analogous to that shown above, with formation of 2-amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate.

EXPERIMENTAL

Diphenyl phosphorylguanidine.* To a solution of 11.2 g (0.192 mole) of guanidine in 50 ml of anhydrous alcohol there was added with energetic stirring and cooling 25.6 g (0.095 mole) of diphenyl chlorophosphonate. The mixture was stirred for thirty minutes longer and was left for five hours at room temperature, after which it was poured into iced water. A colorless oil separated and rapidly crystallized on standing. The crystals were filtered off by suction, washed with ether and dried at 100°. There was obtained 20 g (73%) of diphenyl phosphorylguanidine (diphenyl guanidinophosphate) in the form of colorless crystals; m.p. 118° (from benzene). The literature data [6] give m.p. 118°.

Found %: C 53.25; H 4.83; N 14.77; P. 10.48. $C_{13}H_{14}O_3N_3P$. Calculated %: C 53.61; H 4.84; N 14.43; P 10.63.

2-Diphenylphosphoramido-4-hydroxy-6-methylpyrimidine (I). To the alcoholic solution of sodium ethoxide from 0.58 g (0.025 mole) of sodium and 35 ml of anhydrous alcohol there was added 1.45 g (0.005 mole)

*There is a patent on the preparation of diphenyl phosphorylguanidine by the action of guanidine on the mixture of substances formed by the reaction of 2 moles of phenol with 1 mole of phosphorus oxychloride [6]. However, a check showed that the employment of this technique fails to lead to successful synthesis.

of diphenyl phosphorylguanidine. The solution was heated to boiling and, with stirring, it was treated gradually with 3.25 g (0.025 mole) of freshly distilled acetoacetic ester, after which the mixture was refluxed for four hours longer. The alcohol was distilled in vacuum and the residue was dissolved in the least amount of water. The solution was acidified to Congo red with 5% hydrochloric acid. A heavy yellow oil separated and crystallized on standing. The crystals were filtered off, washed with cold water. There was obtained 0.5 g (28%) of colorless crystals; m.p. 182-183° (from n-butyl alcohol).

Found %: C 56.69; H 4.69; N 11.79; P 8.71. $C_{17}H_{16}O_4N_3P$. Calculated %: C 57.14; H 4.51; N 11.76; P 8.67.

Amino nitrogen in this compound was undetectable. The substance shows absorption in the ultraviolet region (in solution in ethanol) with: wavelength of maximum of 268 mμ, ϵ_{max} 6930; λ_{min} 253 mμ, ϵ_{min} 5450.

One equivalent of alkali is bound in a reaction with dilute alkali; to a sample of the substance there was added an excess of 0.1 N solution of potassium hydroxide, which was then back-titrated with 0.1 N sulfuric acid in the presence of phenolphthalein.

0.0495 g of substance: 1.48 ml 0.1 N KOH; 0.0370 g of substance: 1.10 ml of 0.1 N KOH. Calculated: 1.39, 1.03 ml of 0.1 N KOH.

2-Diphenylphosphoramido-4,6-dihydroxypyrimidine (II). The compound was prepared analogously to the preceding one from 2.9 g (0.01 mole) of diphenyl phosphorylguanidine, 8 g (0.05 mole) of malonic ester, 1.15 g (0.05 g-atom) of sodium and 40 ml of anhydrous alcohol. The mixture was heated for three hours. The residue after evaporation in vacuum was dissolved in the smallest volume of water. After acidification with hydrochloric acid to pH 1 a heavy yellow oil separated and crystallized rapidly after being rubbed. The crystals were thoroughly washed with absolute ether (three 10-ml portions). There was obtained 1.95 g (54%) of colorless crystals with m.p. 159-160° (from chloroform).

Found %: C 53.57; H 3.93; N 11.83; P 8.60. $C_{16}H_{14}O_5N_3P$. Calculated %: C 53.49; H 3.92; N 11.70; P 8.62.

Amino nitrogen was absent in the compound. The substance shows an intense absorption in the ultraviolet region (in solution in ethanol); λ_{max} 258 mμ, ϵ_{max} 19900. One equivalent of base is bound by the substance in reaction with dilute alkali.

2-Diphenylphosphoramido-4,6-dihydroxy-5-ethylpyrimidine (IV). This compound was prepared analogously to the previous one from 2.9 g of diphenyl phosphorylguanidine, 7.52 g of diethyl ester of ethylmalonic acid and 0.92 g of sodium in 40 ml of anhydrous alcohol. Heating lasted for four hours. The residue after evaporation in vacuum was acidified with hydrochloric acid to pH 1. The separated yellowish oil was rubbed with absolute ether. The resulting crystals were filtered off, washed with ether and dried. There was obtained 1.8 g (46.5%) of colorless crystals with m.p. 209-210° (from n-butanol).

Found %: N 10.78, 11.08; P 7.86, 7.74. $C_{18}H_{18}O_5N_3P$. Calculated %: N 10.85; P 7.99.

One equivalent of base is bound by the compound in its reaction with alkali.

Hydrolytic cleavage of 2-diphenylphosphoramido-4,6-dihydroxypyrimidine. a) Aqueous hydrolysis. The compound (II) (0.36 g) was refluxed for one hour with 10 ml of water. Part of the hydrolyzate (5 ml) was acidified with 20% hydrochloric acid to pH 1, extracted with 15 ml of ether, and the ethereal solution was evaporated in vacuum. The residual oil soon crystallized after standing over phosphoric anhydride and potassium hydroxide; the colorless crystals melted at 67-68° and did not give a depressed melting point on mixing with authentic diphenyl hydrogen phosphate [7]. Ultraviolet absorption spectrum of the isolated substance coincides with that of authentic diphenyl hydrogen phosphate (for aqueous solution: λ_{max} 262 mμ, ϵ_{max} 848; λ_{min} 231 mμ, ϵ_{min} 56). On treatment of the compound with ethereal solution of aniline there was obtained a product with m.p. 165°; no depression of melting point was observed with a mixture of the substance with an authentic sample of aniline salt of diphenyl hydrogen phosphate [8]. 2-Amino-4,6-dihydroxypyrimidine and guanidine were

detected chromatographically* in the hydrolyzate (the system used was n-butanol – water). Qualitative tests for phenol and phosphoric acid in the hydrolyzate were negative.

b) Alkaline hydrolysis. The compound (II) (0.1808 g) was refluxed with 10 ml of 1 N sodium hydroxide. In samples of the hydrolyzate the content of amino nitrogen was periodically determined by the Van Slyke method.** After 20 minutes an amount of nitrogen was liberated which corresponded to a 97% hydrolysis of the phosphoramidic bond.

After one hour of heating there were detected in the hydrolyzate by the chromatographic method: 2-amino-4,6-dihydroxypyrimidine, guanidine and diphenyl hydrogen phosphate (system n-butanol – acetic acid – water; 1 : 1 : 1), as well as phenol (in the form of tribromophenol). After hydrolysis for three hours phosphoric acid was detected (by test with ammonium molybdate).

c) Acid hydrolysis. Compound (II) (0.1808 g) was refluxed with 10 ml of 1 N hydrochloric acid. Amino nitrogen was determined periodically in samples of the hydrolyzate. After sixty minutes an amount of nitrogen was liberated which corresponded to 68.7% hydrolysis of the phosphoramidic bond. 2-Amino-4,6-dihydroxypyrimidine diphenyl hydrogen phosphate and guanidine were detected chromatographically in the hydrolyzate (system of n-butanol which was saturated with water), and there were also detected phenol (as tribromophenol) and phosphoric acid (with formation of ammonium phosphomolybdate).

Hydrolytic cleavage of 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine. a) Aqueous hydrolysis. Compound (I) (0.18 g) was refluxed for one hour with 10 ml of water. After cooling of the mixture, the precipitate was filtered off and recrystallized from n-butyl alcohol. Colorless crystals were obtained with m.p. 182-183°, which did not depress the melting point of an authentic and analyzed sample of 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine. No other compounds were detected in the hydrolyzate.

b) Alkaline hydrolysis. Compound (I) (0.1811 g) was refluxed for ten minutes with 10 ml of 1 N sodium hydroxide, after which amino nitrogen was determined in a 0.5-ml sample of the hydrolyzate. This yielded 0.490 ml of nitrogen (24°, 749 mm) which corresponded to 62% hydrolysis. 2-Amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate were detected chromatographically in the hydrolyzate (system of butanol – acetic acid – water). Phenol was detected by a qualitative test with bromine water. Phosphoric acid and guanidine were absent in the hydrolyzate.

c) Acid hydrolysis. The compound (0.1815 g) was refluxed for ten minutes with 10 ml of 1 N hydrochloric acid. In a 0.5 ml sample of the hydrolyzate the content of amino nitrogen was determined. There evolved 0.279 ml of nitrogen (22°, 740 mm) which corresponded to a 44% hydrolysis of the phosphoramidic bond. 2-Amino-4-hydroxy-6-methylpyrimidine and diphenyl hydrogen phosphate were detected chromatographically in the hydrolyzate, along with phenol (as tribromophenol). Phosphoric acid was absent in the hydrolyzate.

SUMMARY

1. A method of synthesis of 2-phosphoramidopyrimidines is suggested, according to which phosphorylated guanidines are condensed with β-dicarbonyl compounds.

2. The following compounds, previously undescribed in the literature, were synthesized: 2-diphenylphosphoramido-4-hydroxy-6-methylpyrimidine; 2-diphenylphosphoramido-4,6-dihydroxypyrimidine; 2-diphenylphosphoramido-4,6-dihydroxy-5-methylpyrimidine; 2-diphenylphosphoramido-4,6-dihydroxy-5-ethylpyrimidine.

3. Hydrolysis of these compounds was studied.

* Here and later we used ascending chromatograms with development of paper No. 2 of the Leningrad Paper Factory. For development of guanidine we used the color test of Weber [9], while the other compounds were developed by means of ultraviolet absorption.

** The determinations were made in the P. G. Ioanisiani apparatus [10]. The determination required five minutes. A control showed that the amino group of 2-amino-4,6-dihydroxypyrimidine is completely determinable in the five minute period.

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CHLOROMETHYLATION OF SATURATED α,ω-PHENYLALIPHATIC ACIDS

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Chloromethylation of saturated α,ω-phenylaliphatic acids is of some interest in connection with research on the synthesis of monomers used to obtain new fibrous polyamides and polyesters. Chromomethylphenylaliphatic acids can be the starting compounds in the synthesis of various α,ω-amino- and α,ω-hydroxycarboxylic acids containing benzene rings on the methylene linkages.

In the present work the chloromethylation of phenylacetic, β-phenylpropionic, γ-phenylbutyric, and δ-phenylvaleric acids of normal structure was carried out; these have not been described as yet in the chemical literature. As in the case of alkylbenzenes [1], this reaction was carried out by passing a stream of hydrogen chloride through a heated mixture of the chloromethylated compound and solution of $ZnCl_2$ in 40% formalin with efficient stirring.

A mixture of ortho and para isomers results from the chloromethylation of phenylaliphatic acids. However, only para isomers were of interest, since the fiber-forming properties were most pronounced in polymers containing para phenyl groups. The saturated p-chloromethylphenylaliphatic acids were separated and purified by crystallizing the reaction products from different solvents. Vacuum distillation was unsuccessful since it was accompanied by polycondensation of the substance with evolution of hydrogen chloride and formation of a yellow viscous tar.

The p-chloromethylphenylacetic, p-chloromethylphenylpropionic, p-chloromethylphenylbutyric, and p-chloromethylphenylvaleric acids obtained were titrated with alkali in a water–alcohol solution; chlorine was quantitatively removed by boiling in an alcoholic $AgNO_3$ solution, and the acids were oxidized to terephthalic acid with 25% nitric acid under pressure (80-90% yield).

EXPERIMENTAL

Chloromethylation of phenylacetic acid. We used 16.0 g of phenylacetic acid, 5.9 g of $ZnCl_2$, and 55.0 g of formalin. The hydrogen chloride was bubbled for 8 hours at a temperature of 75-80°. The resulting suspension was shaken up with a water – chloroform mixture (100 ml of each). The chloroform solution of the substance was washed twice with water and left to stand in the cold for 24 hours. The first portion of p-chloromethylphenylacetic acid that precipitated was filtered out. The mother liquor was concentrated to a volume of 50 ml and mixed with 50 ml of carbon tetrachloride. The second precipitate was combined with the first and recrystallized from a 20 ml chloroform – 20 ml carbon tetrachloride solution. We obtained 5.2 g of p-chloromethylphenylacetic acid, m.p. 152-153° (24% yield).

Found %: C 58.23, 58.30; H 4.82, 4.93; Cl * 18.72, 18.77. Neutralization equiv. 184.3, 183.2. $C_9H_9O_2Cl$. Calculated %: C 58.53; H 4.91; Cl 19.24. Neutralization equiv. 184.6.

Chloromethylation of β-phenylpropionic acid. We used 20.0 g of β-phenylpropionic acid, 3.3 g of $ZnCl_2$, and 32.0 g of formalin. The hydrogen chloride was bubbled for 6.5 hours at a temperature of 75-80°. The resulting suspension was treated with a 100 ml benzene – 50 ml water mixture. The benzene extract was washed twice with water and the solvent distilled off. The residue was then crystallized from 60 and 80 ml. of

*Chlorine content was determined according to Shulz [2].

carbon tetrachloride. We obtained 7.2 g of p-chloromethylphenylpropionic acid, m.p. 118-119° (27% yield).

Found %: Cl 17.55, 17.51; Neutr. equiv. 197.3, 198.8. $C_{10}H_{11}O_2Cl$. Calculated %: Cl 17.88, Neutr. equiv. 198.6.

Chloromethylation of γ-phenylbutyric acid. We used 46.8 g of γ-phenylbutyric acid, 6.6 g of $ZnCl_2$, and 64.0 g of formalin. The hydrogen chloride was bubbled for 5.5 hours at a temperature of 75-80°. The reaction products were treated with a warm mixture of water (100 ml) and dichloroethane (200 ml). The dichloroethane solution was washed twice with water and allowed to stand in cold for 24 hours. The material that precipitated was carefully dried out and recrystallized from 100 ml of dichloroethane. We obtained 20.0 g of p-chloromethylphenylbutyric acid, m.p. 121-122° (33% yield).

Found %: Cl 16.16, 16.32; Neutr. equiv. 209.7, 210.6. $C_{11}H_{13}O_2Cl$. Calculated %: Cl 16.67; Neutr. equiv. 212.6.

Chloromethylation of δ-phenylvaleric acid. We used 20.0 g of δ-phenylvaleric acid, 2.8 g $ZnCl_2$, and 27.0 g formalin. Hydrogen chloride was bubbled for 5 hours at a temperature of 75-80°. The emulsion formed was treated with a water (50 ml) – carbon tetrachloride (40 ml) mixture. The carbon tetrachloride solution of the substance was washed with water, and the solvent distilled off. The residue was dissolved in a 50 ml benzene – 40 ml ligroin solution. The solution was left standing in the cold for 24 hours. The precipitate was recrystallized from a 10 ml benzene – 30 ml ligroin mixture. We obtained 9.9 g of p-chloromethylphenylvaleric acid, m.p. 76-77° (39% yield).

Found %: Cl 15.51, 15.56; Neutr. equiv. 227.0. $C_{12}H_{15}O_2Cl$. Calculated %: Cl 15.67; Neutr. equiv. 226.7.

SUMMARY

The chloromethylation reaction of saturated α,ω-phenylaliphatic acids were carried out. The acids obtained (p-chloromethylphenylacetic, p-chloromethylphenylpropionic, p-chloromethylphenylbutyric and p-chloromethylphenylvaleric) have not been previously described in the chemical literature.

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ORGANOZINC COMPOUNDS AS CATALYSTS IN THE POLYMERIZATION OF PROPYLENE

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When Natta [1] used Ziegler's catalyst [2] ($Al(C_2H_5)_3 + TiCl_4$) to polymerize propylene, he obtained at first a solid polypropylene. The literature contains information [3] on the use of other group II and III metals (Be, In, Ga, Mg, Cu, Zn) in connection with similar organic reactions; however, no systematic investigation of their catalytic properties has been conducted.

We thought it might be of some interest to study the catalytic activity of organo-zinc compounds (diethyl-, dipropyl-, and diphenylzinc) in propylene polymerization. Diethylzinc with an addition of titanium tetrachloride proved to be active. In the presence of diethylzinc and stannic chloride (or isopropyl sodium) propylene did not polymerize. The effects of reaction temperature, duration, catalyst composition (the molar ratio of $Zn(C_2H_5)_2$ and $TiCl_4$, later denoted as K), and solvent on the polymerization of propylene were investigated. We showed that the best yield of polypropylene is obtained at 110-120° (Table I).

TABLE 1

The Effect of Temperature on the Polymerization of Propylene. Conditions: Solvent – 3 ml of isooctane; K = 1

$Zn(C_2H_5)_2$ (g)	$TiCl_4$ (g)	C_3H_6 (g)	Temperature	Time (in hours)	Yield of polymer (g)	%
0.26	0.40	1.37	90—95°	3	0.60	43.7
0.12	0.24	1.41	100—105	3	0.85	60.2
0.25	0.39	2.77	110—120	3	2.00	73.0
0.26	0.40	2.87	110—120	5	2.32	83.0
0.12	0.19	1.56	130—140	5	0.70	43.8

When polymerization time was increased from 3 to 5 hours, the increase in polypropylene yield was insignificant (Table I).

It was shown that composition of the catalyst has a great effect on the yield and type of polymer formed. The percent of propylene converted into polymer was largest at the equimolar ratio of $Zn(C_2H_5)_2$ and $TiCl_4$, but the polymer obtained in this case was an oil of varying viscosities. At K = 3 a 30% yield of a hard polymer was obtained (m.p. 150-158°, mol. wt., 10,000-18,000.* If K is further increased the yield of solid polymer noticeably decreases (Table 2).

Heptane and isooctane (2,2,4-trimethylpentane) were tried as solvents in the polymerization of propylene. We determined that in heptane the yield is slightly lower than in isooctane (Table 3).

* The molecular weight was calculated using the formula $M = \frac{\eta}{2.5 \cdot 10^{-5}}$ [7], where η, the specific viscosity in tetralin, equals 0.29-0.47.

TABLE 2

The Effect of $Zn(C_2H_5)_2 - TiCl_4$ Molar Ratio (K) on the Yield of Polypropylene. Conditions: 110-120°, reaction time 3 hours

$Zn(C_2H_5)_2$ (g)	$TiCl_4$ (g)	K	C_3H_6 (g)	Polymer yield (g)	Polymer yield %	The outside appearance of polymer
0.33	0.66	0.8	1.80	1.29	72.6	Oil
0.22	0.36	0.9	1.77	1.11	62.7	Oil
0.25	0.39	1.0	2.77	2.30	83.0	Oil
0.30	0.47	1.0	2.97	1.77	59.6	Viscous oil
0.25	0.19	2.0	0.82	0.21	25.6	Semisolid
0.30	0.17	3.0	2.94	0.75	25.0	Solid
0.23	0.12	2.9	2.90	0.89	30.0	Solid
0.26	0.09	4.4	2.43	0.28	11.5	Solid
0.25	0.06	6.4	2.05	0.15	7.5	Solid
0.22	0.04	8.5	1.70	—	—	—
0.30	0.0	—	1.80	—	—	—
0	0.16	—	1.41	0.02	1.4	Traces of oil

TABLE 3

The Effect of Solvent on the Polymerization of Propylene. Conditions: 110-120°, reaction time 3 hours

$Zn(C_2H_5)_2$ (g)	$TiCl_4$ (g)	K	Solvent (in (ml)	C_3H_6 (g)	Polymer yield g	Polymer yield %	The outside appearance of polymer
0.22	0.36	0.92	0	1.77	1.11	62.7	Oil
0.21	0.29	1.15	Heptane 2.04	1.32	0.74	56.0	Oil
0.26	0.28	1.40	1.96	1.34	0.44	32.8	Semisolid
0.12	0.23	0.90	Isooctane 2.13	1.41	0.85	60.2	Oil
0.26	0.30	1.50	2.15	1.37	0.50	36.2	Semisold
0.26	0.18	2.50	2.08	1.30	0.24	18.6	Solid
0.25	0.13	2.50	0.95	2.27	0.65	29.0	Solid
0.30	0.17	3.00	0.96	2.94	0.75	25.0	Solid

When diethylzinc is replaced with dipropyl- and diphenylzinc, the change in the activity of the catalyst, in connection with propylene polymerization, was insignificant. Hence, the nature of the radical shows only small influence on the catalytic ability of the organozinc compound. For the $Zn(C_3H_7)_2 + TiCl_4$ catalysts the effect of molar ratio of the components on yield and type of polymer were investigated (Table 4, 5).

TABLE 4

Propylene Polymerization Using $Zn(C_3H_7)_2 + TiCl_4$ atalyst. Conditions: 110-120°, reaction time 5 hours, solvent – 1 ml of isooctane

$Zn(C_3H_7)_2$ (g)	$TiCl_4$ (g)	K*	C_3H_6 (g)	Polymer yield g	Polymer yield %	The outside appearance of polymer
0.17	0.22	1.0	1.79	0.95	52.5	Oil
0.17	0.22	1.0	2.49	1.21	48.6	Oil
0.20	0.22	1.17	2.15	0.86	40.5	Viscous oil
0.16	0.11	2.0	1.68	0.35	20.8	Semisolid
0.17	0.07	3.0	1.82	0.27	15.2	Solid
0.17	0.05	3.7	1.83	0.20	11.3	Solid
0.32	0.04	10.0	1.25	—	—	—

*K – molar ratio of $Zn(C_3H_7)_2$ and $TiCl_4$.

TABLE 5

Propylene Polymerization Using $Zn(C_6H_5)_2 + TiCl_4$ Catalyst. Conditions: 110-120°, reaction time, 5 hours solvent – 1 ml of isooctane

$Zn(C_6H_5)_2$ (g)	$TiCl_4$ (g)	K*	C_3H_6 (g)	Polymer yield		The outside appearance of polymer
				g	%	
0.20	0.17	1.0	2.50	1.63	65.0	Oil
0.24	0.11	1.9	2.70	1.67	62.3	Oil
0.22	0.11	2.0	2.45	1.22	50.0	Viscous oil
0.25	0.07	3.0	2.50	0.54	23.0	Semisolid
0.36	0.08	3.7	2.52	0.44	17.5	Solid
0.38	0	—	2.50	—	—	

EXPERIMENTAL

Starting Materials. Popylene was obtained by dehydrating isopropyl alcohol over aluminum oxide at 350-400° and carefully purified to remove contaminants. Diethylzinc was obtained from a Zn-Cu alloy and a mixture of bromo and iodoethane [4] (b.p. 30-32° (5 mm)). Dipropylzinc was synthesized in the same fashion as diethylzinc (b.p. 39-40° (9 mm)). The organozinc compounds were used in the form of concentrated isooctane solutions (55-60%). Diphenylzinc was obtained using A. N. Nesmeianov's method of preparation [5], (m.p. 107-109°. The solvents used (chemically pure heptane and isooctane) were in addition dried over sodium.

Polymerization was conducted in molybdenum – glass ampules of about 10 ml capacity. Dry and clean ampules were filled with purified nitrogen. A weighed portion of catalyst and solvent was placed in the ampule. Then a fixed quantity of propylene (1.5-2 g) was condensed into the ampule. A special set-up [6] was used to fill the ampules with nitrogen and condense the propylene. The filled ampules were placed in an electric furnace which was attached to a shaker, and heated to a fixed temperature. At this temperature the contents of the ampules were agitated for 3-5 hours. When polymerization was completed, the ampules were cooled and open. The propylene remaining was evaporated by carefully warming the ampules to room temperature. The contents were poured out into methanol which was then acidified with dilute hydrochloric acid (to destroy the catalyst), and the polymer would precipitate out of solution. The percent of propylene converted into polymer was determined by difference in weight of original and residual propylene. The yield of solid polypropylene was determined directly by weighing the polymer.

SUMMARY

1. The catalytic activity of diethylzinc with addition of titanium tetrachloride was investigated in connection with the propylene polymerization reaction. The optimum conditions for obtaining a solid polypropylene were determined.

2. It was shown that in the propylene polymerization reaction the activity of catalysts containing dipropyl or diphenylzinc shows only insignificant change from the activity of those containing diethylzinc.

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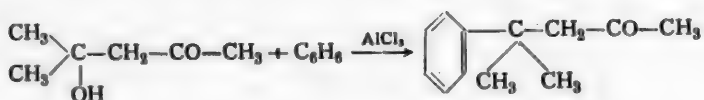
CONDENSATION OF DIACETONE ALCOHOL WITH BENZENE

I. P. Labynskii

In recent years I. P. Tsukervanik and co-workers have been conducting a systematic study of condensations between two-functional aliphatic compounds (1,3-butylene chlorohydrin and 1,3-butylene glycol [1], 1,4-pentanediol [2], tertiary diols [3] and aromatic compounds in order to learn the exchange activity of various functional groups. In accordance with the mutual atomic interaction theory [4], a decrease in the interaction of functional groups was detected in the cases where the groups were farther apart. Since they possess theoretical significance, such studies should show new synthetic routes.

We decided to run a condensation of benzene with diacetone alcohol, which has an alcohol group β to the ketonic. Only Niederl's work [5] on condensation of diacetone alcohol with phenol in the presence of $ZnCl_2$ is found in the literature.

One could expect that in diacetone alcohol the alcohol group would react alone or simultaneously with the ketonic group. It appears that when diacetone alcohol is condensed with benzene in the presence of 2 moles of $AlCl_3$, under mild conditions the reaction proceeds at first according to this equation:



(I)

with the formation of 2-phenyl-2-methylpentanone-4 (I) (60.7% yield) and a crystalline substance melting at 127° (II). An increase in temperature or prolongation of the reaction tends to increase the yield of the crystalline product (II).

A separate experiment in which (I) was heated with $AlCl_3$ gave the same product melting at 127° (II). This experiment confirms the secondary origin of substance (II), and consequently shows that condensation proceeds only through the alcohol group.

Some authors [6, 7] obtained the arylketone (I) by condensing mesityl oxide with benzene in the presence of $AlCl_3$. Considering that diacetone alcohol is half as expensive as mesityl oxide, it is more advantageous to obtain the arylketone (I) by our method.

We think, that in analogy the mesityl oxide [7] diacetone alcohol can be condensed with other aromatic hydrocarbons possessing ring hydrogens more active than benzene; in this way various aromatic ketones would be obtained.

EXPERIMENTAL

From a number of experimental runs only one (that which gave best results) is cited. To a mixture containing 20 g of diacetone alcohol (prepared according to [8]) and 100 ml of benzene, 46 g of $AlCl_3$ was gradually added during 1 hour at 5° with stirring. Subsequently the stirring was continued for 1 hour at 25°. The reaction mixture was decomposed with acidified water, the upper layer separated and dried over Na_2SO_4 then distilled at 20 mm. Fractions obtained: 1st 60-127°, 2.1 g; 2nd 128-130°, 21.3 g (60.7%); 3rd 131-200°, 2.9 g (8.7%); residue 0.5 g.

2nd fraction represented 2-phenyl-2-methylpentanone-4 (I).

n_D^{20} 1.5100, d_4^{20} 0.96800, MR_D 54.3; calculated 54.0. Oxime (from alcohol: m.p. 51-52°). Literature data, see [9].

3rd fraction crystallized immediately, m.p. 127° (from benzene).

We heated 5.0 g (I) with 3.8 g of $AlCl_3$ in a petroleum ether solution on a water bath during 2 hours. After the usual treatment 1.7 g of crystalline substance, m.p. 127° (from benzene), were obtained.

This sample when mixed with the substance obtained during condensation did not produce any lowering of the melting point. Substance (II) was not further investigated.

SUMMARY

It was shown that benzene could be alkylated with diacetone alcohol in the presence of $AlCl_3$ and that 2-phenyl-2-methylpentanone-4 was formed.

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SYNTHESIS OF ORGANOPHOSPHORUS COMPOUNDS FROM HYDROCARBONS AND THEIR DERIVATIVES

VIII. A STUDY OF OXIDATION OF PHOSPHORUS TRICHLORIDE BY OXYGEN

M. K. Baranaev, Iu. M. Zinov'ev, T. K. Skripach
and L. Z. Soborovskii

Oxidative chlorophosphonation of hydrocarbons and their derivatives is a conjugated reaction as the result of which compounds containing a phosphorus – carbon bond preformed. Simultaneously there occurs the oxidation of the phosphonating agent used, $XPCl_2$ (X = chlorine, alkyl or aryl residues, alkoxy, dialkylamino or other monovalent organic groups) to the corresponding compounds of quinquevalent phosphorus: $RH + 2XPCl_2 + O_2 \rightarrow RP(O)XCl + XP(O)Cl_2 + HCl$.

Oxidative chlorophosphonation is applicable to various classes of hydrocarbons and their derivatives [1-6]. In all cases the process of formation of a phosphorus-carbon begins evidently with oxidation of phosphorus trichloride.

Few studies are extant in which oxidation of phosphorus trichloride by oxygen has been studied. There are only the indications by Remsen of the possibility of oxidation of phosphorus trichloride by ozonized oxygen [7]* and a patent with a description of "burning" at 150° of a gaseous mixture of phosphorus trichloride and oxygen taken in 2:1 molar proportion [9].

Our observations show that oxidations of both the phosphorus trichloride itself and of the compounds formed from it and corresponding to the formula $XPCl_2$ are readily realized by the simple passage of gaseous oxygen or air through the appropriate reactants.

Previously a supposition was expressed about the radical character of both the oxidative chlorophosphonation and the oxidation of pure phosphorus trichloride [10]. According to this supposition the primary act in the oxidation of phosphorus trichloride is the addition of a molecule of oxygen to phosphorus trichloride. The resulting adduct may be regarded as a biradical ($Cl_3\dot{P}O\dot{O}$) or as a bipolar ion ($Cl_3\overset{+}{P}O\overset{-}{O}$): $PCl_3 + O_2 \rightarrow Cl_3\dot{P}O\dot{O}$.

In the case of oxidation of pure phosphorus trichloride this adduct reacts immediately with a second molecule of phosphorus trichloride and forms phosphorus oxychloride: $Cl_3\dot{P}O\dot{O} + PCl_3 \rightarrow 2POCl_3$.

Thus all of the phosphorus trichloride is gradually converted into phosphorus oxychloride, i.e. the process is completed. However if a hydrocarbon (RH) is present in the reaction mixture, the possibility arises of involvement of the latter in the reaction.

Biradical $Cl_3\dot{P}O\dot{O}$ colliding with a molecule RH forms an organic radical R· and a radical OH: $Cl_3\dot{P}O\dot{O} + RH \rightarrow POCl_3 + R\cdot + \dot{O}H$. These radicals may account for the origin of the phosphorous-carbon bond and may lead to the formation of chlorides of the corresponding alkylphosphonic acids.

Oxidative chlorophosphonation may be regarded, therefore, as an example of conjugated oxidation which proceeds according to the scheme which resembles that proposed by N.A. Shilov [11] for processes of autooxidation.

*Evidently this paper served as the basis for Nekrasov's assertion about the difficulty of oxidation of phosphorus trichloride by oxygen which allegedly requires the presence of ozone or the use of a catalyst [8].

According to Shilov'sconcepts, a conjugation of reactions is possible only in those cases in which there exists an intermediate substance which connects the primary and the secondary processes. At the same time a charac-

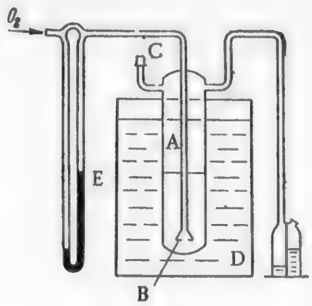

Fig. 1. Scheme of apparatus.

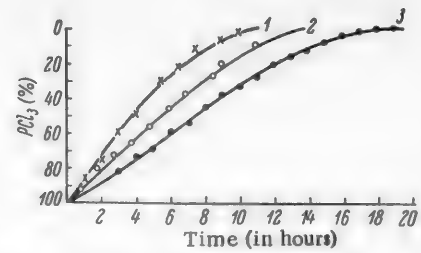

Fig. 2. Oxidation of PCl_3 at constant temperature (25°) with varying stirring. Volume of PCl_3 (in ml.): 1) 25, 2) 50, 3) 60.

teristic peculiarity of conjugated reactions (in contrast to catalytic reactions) is their low order of dependence on the conditions under which the interaction of the reactants takes place.

For a better understanding of the complex process of formation of the phosphorus – carbon bond it appeared reasonable to study the reaction of oxidation of phosphorus trichloride in more detail.

It is shown in the present work that the above-described scheme of oxidative chlorophosphonation agrees well with facts which are observed during the oxidation of phosphorus trichloride by gaseous oxygen under various conditions. A study of the kinetics of oxidation of phosphorus trichloride was made not only with pure PCl_3, but also in the presence of iodine and for a mixture with cyclohexane. The study of oxidation of phosphorus trichloride by oxygen in the presence of iodine was undertaken since it had been noted previously that in such a case the oxidative phosphonation is hindered (an analogous effect is caused by ferric chloride, nitrobenzene and some other reagents) [1]. Introduction of cyclohexane into the reaction should permit one to observe the process under the conditions which lead to the formation of the C–P bond.

Oxidation of phosphorus trichloride was run in vessel A (Fig. 1), provided with a gas inlet tube with a porous glass plate B and opening C, closed by a ground-in stopper. Vessel A is placed in a thermostat D, which assures the temperature level desired for the experiment with an accuracy of $\pm$ 0.1°. Into vessel A there was placed a known volume of freshly-distilled phosphorus trichloride and oxygen was passed in, the rate of flow of which was controlled by the flowmeter E. The content of trivalent phosphorus in phosphorus trichloride was determined before the start of the experiment. After predetermined time intervals, samples were taken in which the content of trivalent phosphorus was determined (iodometrically). The rate of passage of oxygen was constant in all experiments (0.05 liter per minute). Oxidation was run at various temperatures (0, 25 and 40°). In order to make observation on the effects of stirring on the process possible, various amounts of phosphorus trichloride (25, 50 and 60 ml) were used for the reaction. In the presence of additives (cyclohexane and iodine) the oxidation was realized in all cases at 25° while the liquid volume was held at 25 ml. The experimental results are shown in Figs. 2-4.

Curves which show the degree of oxidation of phosphorus trichloride with time indicate that the process proceeds at a constant rate which changes only with conditions of agitation until some 60-70% of the reactant taken had been oxidized. The rate of oxidation in this period is greater, the better are the conditions of agitation (Fig. 2). Thus, the reaction of oxidation of phosphorus trichloride by gaseous oxygen is a heterogeneous process, the rate of which is determined, at least in the initial stage, by the rate of dissolution of oxygen. All factors which aid the acceleration of absorption of oxygen by the liquid phase should accelerate the oxidation.

Increased rate of oxidation in the presence of cyclohexane may be explained also by the greater rate of absorption of oxygen from the gaseous phase under these conditions.

With decrease of the concentration of phosphorus trichloride in the liquid phase from the initial value to 40-30%, the rate of oxidation declines. During this period, the rate of dissolution of oxygen probably does not change materially and a gradual accumulation of it in the liquid takes place. In this stage the course of

the process of oxidation is determined not only by the rate of passage of oxygen through the interface of gas and liquid, but also by the rate of its reaction with phosphorus trichloride in the homogeneous liquid phase. Thus, for example, the rates of oxidation of phosphorus trichloride with added cyclohexane and without the latter are almost the same at equal concentrations of the unoxidized material (less than 30% of the initial value) (Fig. 3). This additionally confirms the supposition that the process of phosphonation proceeds through the formation of a product of addition of oxygen to phosphorus trichloride.

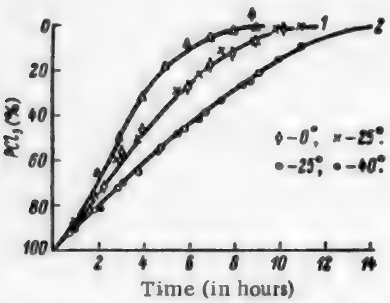

Fig. 3. Oxidation of PCl_3 at various temperatures. Volume of PCl_3: 1) 25 ml, 2) 50 ml, 4) PCl_3 + 25 ml C_6H_{12} at 25°.

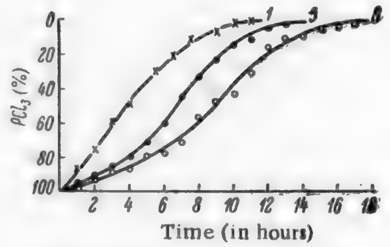

Fig. 4. Oxidation of PCl_3 in the presence of iodine (25 ml, 25°). 1) Without iodine, 5) 0.005% iodine, 6) 0.01% iodine.

Insignificant (0.05-0.02%) additions of iodine greatly hinder the oxidation. The solubility and the rate of absorption of oxygen evidently cannot be changed significantly as the result of addition of such small amounts of iodine. Consequently, in this case the slowest process is the homogeneous reaction of oxidation of phosphorus trichloride by the dissolved oxygen. The S-shaped course of the curves of oxidation of phosphorus trichloride with addition of 0.01 and 0.005% of iodine indicates that iodine, as a negative catalyst, is gradually consumed – leached out from the solution by the excess oxygen or is neutralized in the process of the reaction (Fig. 4).

In agreement with the supposition regarding the heterogeneous nature of the process of oxidation of pure phosphorus trichloride, one may expect some insignificant changes of its rate with alteration of temperature. This supposition is completely confirmed by experiment. The rate of reaction at 0, 25 and 40° is practically the same (Fig. 3).

However, the rate of oxidation is independent of temperature not only in the initial phase, but also after the rate of the whole process begins to depend on the amount of unreacted phosphorus trichloride. Therefore, the rate of the homogeneous reaction of oxidation of phosphorus trichloride by the dissolved oxygen is also practically independent of temperature. This shows that the energy of activation of oxidation of phosphorus trichloride is very small and the process, evidently, has the free radical character, proceeding by the scheme shown above, with intermediate formation of the radical $Cl_3\dot{P}O\dot{O}$.

SUMMARY

1. The initial stage of oxidation of phosphorus trichloride by gaseous oxygen is a heterogeneous process, the rate of which is determined by the rate of dissolution of oxygen.

2. The rate of oxidation of phosphorus trichloride by gaseous oxygen is practically independent of temperature both in the beginning and at the end of the process.

3. The activation energy of oxidation of phosphorus trichloride by oxygen is very small, which agrees with the supposition about the free radical character of this process.

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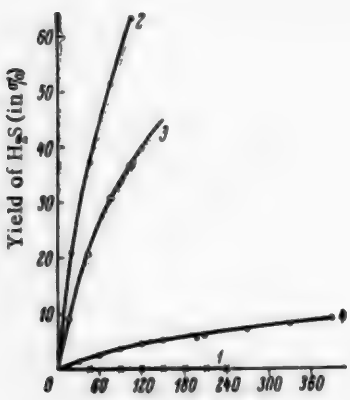
REACTIONS OF FREE RADICALS IN SOLUTION

XIV. FORMATION OF FREE RADICALS IN DECOMPOSITION OF HYDROGEN DISULFIDE AND THEIR REACTIONS WITH α- AND β-OLEFINS

E. I. Tiniakova, E. K. Khrennikova and B. A. Dolgoplosk

A series of papers devoted to the study of reactivity of free radicals with α- and β-olefins have been appearing recently. Reactions of alkyl free radicals with α-olefins proceed mainly in the direction of their addition to the double bonds with a corresponding decrease of the role of reactions of hydrogen cleavage [1]. In case of β-olefins the predominant reaction of the methyl radical is the cleavage of a hydrogen atom with formation of methane [14]. Analogous data have been obtained also for the radical with the reactive center on the nitrogen atom $(CH_3)_2N\cdot$ [2]. Reactions of free radicals of type $RO^{\cdot}$ and $RO_2{\cdot}$ with various olefins mainly proceed in the direction of cleavage of a hydrogen atom with formation of the corresponding alcohols and hydroperoxides [3].

The present communication is devoted to the study of reactivity of $\cdot SH$ radicals with α- and β-olefins; this study has a real interest in its connection with their role in the process of vulcanization with sulfur [4].



Decomposition of hydrogen disulfide in ethylbenzene solution at 70° in quartz ampul in nitrogen atmosphere (H_2S concentration in solution is 2 weight %). 1) in NO atmosphere, 2) freshly prepared H_2S_2, 3) H_2S_2 treated with HCl for 3 hours, 4) H_2S_2 stored under HCl for 3 weeks.

As the source of $\cdot$ SH radicals, we used hydrogen disulfide which as is known, decomposes readily with formation as end products of hydrogen sulfide and sulfur. The decomposition of hydrogen disulfide proceeds particularly intensively in the presence of alkalis, amines and other compounds of basic character [5]. The reaction is retarded in the presence of dilute mineral acids, especially hydrochloric, as a result of which fact hydrogen disulfide is generally stored in an atmosphere of dry hydrogen chloride. In such organic solvents as xylene, toluene, ethylbenzene, isopropylbenzene, etc., the decomposition also proceeds with liberation of equivalent amounts of hydrogen sulfide and sulfur; in this case the decomposition occurs with considerably greater speed in ampuls made of ordinary glass than in quartz vessels [4]. The rate of decomposition of hydrogen disulfide decreases with increased duration of the time of its storage in the atmosphere of hydrogen chloride (see figure). In a solution of rubber in the same solvents the decomposition proceeds without an observable liberation of hydrogen sulfide, while the effect of vulcanization (gel formation) is seen [4].

Evidently, the decomposition of hydrogen disulfide, analogously to that of hydrogen peroxide, proceeds by a chain mechanism through the stage of $\cdot$ SH and $\cdot S_2H$ radicals; here the sulfhydryl radicals, in contrast to the majority of aliphatic and hetero-radicals, do not participate in the reaction with the solvent. The absence of reaction $\cdot SH + AH \rightarrow H_2S + A\cdot$ (where AH is the solvent) indicates the equimolar ratio of amounts of sulfur and

hydrogen sulfide formed in the decomposition of hydrogen disulfide. The formation of equivalent amounts of sulfur and hydrogen sulfide on thermal decomposition of hydrogen disulfide may be connected only with reactions of disproportionation and chain transfer:

$$\begin{gathered}
HSSH \rightarrow HS\cdot + \cdot SH \\
HS\cdot + HSSH \rightarrow H_2S + HS_2\cdot \\
HS_2\cdot + HS\cdot \rightarrow H_2S + S_2 \text{ (or } H_2S_2 + S) \\
HS\cdot + HS\cdot \rightarrow H_2S + S
\end{gathered}$$

The radical character of the reaction is also confirmed by the data obtained by us on the composition of hydrogen disulfide in the presence of a free-radical acceptor – nitrogen oxide (figure). On heating hydrogen disulfide in ethylbenzene solution at 70° under conditions of a continuous passage of gaseous NO through the solution, the decomposition proceeds without liberation of hydrogen sulfide. It was shown previously that hydrogen sulfide does not react with NO under the indicated conditions for the reaction.

In decomposition of hydrogen disulfide in the absence of olefins there may develop two competing directions of reaction:

$$HS\cdot(HS_2\cdot) \longrightarrow \begin{cases} \xrightarrow{\text{Disproportionation}} H_2S + \text{sulfur} \\ \xrightarrow[\text{Addition to C=C bond}]{} RS_nR \end{cases}$$

We studied the decomposition of hydrogen disulfide in various olefins containing terminal and internal double bonds.

The relative reactivity of hydrogen disulfide and olefins and the character of the reactions which occur were evaluated by the amount of hydrogen sulfide liberated and by the composition of the resulting addition

TABLE 1

Yield of H_2S in Decomposition of Hydrogen Disulfide in Ethylbenzene and Olefins

Solvent	Temperature	Yield of H_2S (in % of theoretical)*
Ethylbenzene	70°	97-98
Isoprene	70	2.0
Styrene	70	5.0
α-Pentene	50	9.0-10.8
α-Pentene	130	5.2
β-Pentene	50	42-48
Cyclohexene	50	59.2-62.0

products. The results are shown in Tables 1 and 2. If follows from the data in Table 1 that during the decomposition of hydrogen disulfide in olefins containing a vinyl double-bond (α-pentene styrene, isoprene), the reaction of formation of hydrogen sulfide is almost completely repressed. In cases of olefins with an internal double bond (β-pentene, cyclohexene) which are weaker acceptors of free radicals, the decomposition of hydrogen disulfide is accompanied by formation of hydrogen sulfide, the amount of which, however, is much smaller than in decomposition in inert solvent.

The products of reaction of hydrogen disulfide with α- and β-pentenes, as well as cyclohexene, were isolated and characterized as models of the structure of the cis-1,4 link of polybutadiene (Table 2). From data

*Theoretical yield was taken as the amount of H_2S formed by equation: $H_2S_2 \rightarrow H_2S + S$.

In this table it follows that in decomposition of hydrogen disulfide in α-pentene the main product of the reaction is a monosulfide, the yield of which is 30-40%. Along with the monosulfide there were isolated and characterized the diamyldisulfide and diamyltetrasulfides,as well. The total yield of isolated mono-, di- and tetrasulfides was about 75%. In β-olefins (β-pentene, cyclohexene), the reaction also leads to the formation of sulfides (mono-, di- and tetra-), the total yield of which, however, is considerably below the yield of these products in the decomposition run in α-olefins, owing to the parallelly-running course of the process of formation of hydrogen sulfide. The summary yield of isolated sulfides and hydrogen sulfide after the reaction in β-pentene was 58%, and after the reaction in cyclohexene it was about 50%. The higher yield of alkyl sulfides in the case of decomposition of hydrogen disulfide in α-pentene corresponds to its greater reactivity in reactions with free radicals. The yields of various alkyl sulfides after decomposition of hydrogen disulfide in α- and β-olefins were rather close after recalculation to the amount of H_2S_2 which had added, this fact indicating the similar mechanism of their formation.

TABLE 2

Composition of Products of the Reaction of Hydrogen Disulfide with Olefins (Temperature 50°, duration of reaction 15 hours)

Reaction product	α-Pentene(conc.of H_2S_2 1.08 mole/liter)		β-Pentene(conc. of H_2S_2 1.18 mole/liter)		Cyclohexene(conc. of H_2S_2 1.01 mole/liter)	
	Content of sulfur in the product, %					
	Calc. on sulfur introduced as H_2S_2	Calc. as sulfur in added H_2S_2	Calc. as sulfur introduced as H_2S_2	Calc. as sulfur in added H_2S_2	Calc. on sulfur introduced as H_2S_2	Calc. on sulfur in added H_2S_2
H_2S	4—5	—	21	—	29—31	—
RSH	0.5—1	0.55	0	—	3.2	8.0
R_2S	31—39	34.5	14.9	25.7	7.75	9.5
R_2S_2	10	11.1	3.0	5.2	7.42	18.5
R_2S_4	25	27.8	18.7	32.4	—	—
$R_2S_n + S$	18	—	30.9 **	—	42.4	—

The formation of sulfides in the decomposition of hydrogen disulfide in olefins may be connected only with the participation in the reactions of free radicals.

The most probable mechanism of the reaction is shown in the scheme below.***

a) Initiation stage.

$$HSSH \longrightarrow 2 \cdot SH.$$

b) Formation of monosulfide.

$$ACH{=}CH_2 + \cdot SH \rightarrow A\dot{C}H{-}CH_2SH \xrightarrow{HSSH} ACH_2{-}CH_2SH + HS_2 \cdot \rightarrow$$
$$\xrightarrow{R\cdot} RH + ACH_2{-}CH_2S \cdot \xrightarrow{ACH=CH_2} ACH_2{-}CH_2S{-}CH_2{-}\dot{C}HA \xrightarrow{HSSH}$$
$$\longrightarrow ACH_2{-}CH_2{-}S{-}CH_2{-}CH_2A.$$

*Amount of H_2S which had added was determined by the difference between the introduced hydrogen disulfide and that consumed in formation of sulfur and hydrogen sulfide, which always formed in the reaction in equivalent amounts.

** 15.6% of crystalline sulfur, with m.p. 114°, was isolated from the mixture.

*** Under the conditions of the reaction, prepared hydrogen sulfide does not add to olefins.

c) Formation of disulfides:

1) Recombination of radicals.

$$2ACH_2{-}CH_2S\cdot \longrightarrow ACH_2{-}CH_2S{-}SCH_2{-}CH_2A,$$

$$2)\ ACH{=}CH_2 + \cdot S_2H \rightarrow A\underset{\cdot}{C}HCH_2SSH \xrightarrow{HSSH} ACH_2CH_2SSH \xrightarrow{R\cdot}$$

$$\longrightarrow ACH_2CH_2SS\cdot \xrightarrow{ACH=CH_2} ACH_2{-}CH_2{-}SS{-}CH_2{-}\underset{\cdot}{C}HA \xrightarrow{HSSH}$$

$$\longrightarrow ACH_2CH_2{-}S{-}S{-}CH_2{-}CH_2A.$$

d) Formation of tetrasulfides.

$$2ACH_2CH_2SS\cdot \longrightarrow ACH_2CH_2{-}SSSS{-}CH_2CH_2A \text{ etc.}$$

EXPERIMENTAL

Hydrogen disulfide was prepared by fractional distillation of hydrogen polysulfide in vacuum [6]. B.p. 75°, d_4^{15} 1.715. In all cases freshly prepared hydrogen disulfide was used for the study of the reaction in olefins.

α-Pentene was prepared from ethyl bromide and allyl bromide [7]. B.p. 30°, n_D^{20} 1.3720.

β-Pentene was prepared by dehydration of secondary amyl alcohol [8]. B.p. 35.5° at 736 mm, n_D^{20} 1.3790.

Cyclohexene was prepared by dehydration of cyclohexanol [9]. B.p. 83.5°, n_D^{20} 1.4453.

The olefins were thoroughly dried and were distilled through a column directly before the experiment.

The reaction of hydrogen disulfide with olefins was run in sealed ampuls in a nitrogen atmosphere. For protection of H_2S_2 from a premature decomposition the ampuls were preliminarily kept for several hours in the atmosphere of dry gaseous hydrogen chloride. After this, the ampuls were pumped out several times with an oil pump, were filled with dry nitrogen, after which the solution of H_2S_2 was introduced countercurrent to the stream of nitrogen, the solution having been prepared directly before the experiment in a quartz flask.

The sealed ampuls were heated in a thermostat at 50° for 15 hours. After completion of the reaction, the ampuls were cooled to −70°, were opened, connected to an absorption system for taking up hydrogen sulfide (cadmium chloride solution), and a stream of nitrogen was passed through the solution at 0° for the removal of hydrogen sulfide, which was then determined iodometrically [10].

Individual samples of the solution, after the removal of H_2S from it, were analyzed for the content of mercaptan and for the completeness of decomposition of H_2S_2. For determination of completeness of decomposition of H_2S_2, several milliliters of the solution were shaken with 10% solution of cadmium chloride, with which H_2S_2 forms a precipitate of CdS_2. In all experiments CdS_2 was absent, which fact indicates the complete decomposition of hydrogen disulfide.

The solvent was distilled from the reaction mixture at atmospheric pressure, and the residue was fractionated in vacuum. The resulting crude sulfides were again distilled. Elemental composition, index of refraction and density at 15°, molecular weight by cryoscopic method, functional groups (SH, S, S-S) [12] and unsaturation by means of IBr solution in carbon tetrachloride [11], were determined for the reaction products after their isolation in the pure state. The disulfides were reduced with zinc dust in acetic acid and the resulting mercaptan was determined argentometrically [12]. The polysulfides were treated by boiling with sodium sulfite for the removal of elemental and polysulfide sulfur [13]. The disulfide formed thereby was determined argentometrically [12]. The monosulfide sulfur was determined by bromination [12].

Reaction of H_2S_2 with α-pentene. There was taken 3.05 g of H_2S_2 in 50 ml of α-pentene. There was isolated: a) H_2S 0.19 g (5.4% of the theoretical amount*).

*In all cases the theoretical amount was taken as the amount of product (H_2S, mono-, di- and tetrasulfide) which could form from all sulfur contained in the H_2S_2 taken.

b) Diamyl monosulfide 4.78 g. (31.0%).

B.p. 86-87° at 12-13 mm, d_4^{15} 0.8446, n_D^{15} 1.4572.

Found %: C 68.44; H 12.72; S 18.37. M 171. Iodine number 0; content of monosulfide sulfur 10%. $(C_5H_{11})_2S$. Calculated %: C 68.96; H 12.64; S 18.39. M 174.

c) Diamyl disulfide 0.94 g (11.8%).

B.p. 68-75° at 1 mm, d_4^{15} 0.9381, n_D^{15} 1.5038.

Found %: C 58.20; H 10.58; S 30.44. M 198, 201; Iodine number 0; content of disulfide sulfur 102%. $(C_5H_{11})_2S_2$. Calculated %: C 58.25; H 10.68; S 31.07. M 206.

d) Diamyl tetrasulfide 1.7 g (25%).

B.p. 100-107° at 1 mm, n_D^{20} 1.5285.

Found %: C 43.84; H 8.92; S 47.25. M 268; Iodine number 0. $(C_5H_{11})_2S$. Calculated %: C 44.44; H 8.15; S 47.40. M 270.

e) Residue after distillation was a mixture of sulfur with a small amount of the tetrasulfide and possibly still higher polysulfides.

Reaction of H_2S_2 with β-pentene. There was used 5.6 g of H_2S_2 in 50 ml of β-pentene. There were isolated: a) H_2S 1.17 g (21%).

b) Diamyl monosulfide 4.26 g (14.9%).

B.p. 79° at 10 mm, d_4^{15} 0.8426, n_D^{15} 1.4568.

Found %: C 69.38; H 12.61; S 18.68. M 173; iodine number 0; content of monosulfide sulfur 99.7%. $(C_5H_{11})_2S$. Calculated %: C 68.96; H 12.64; S 18.39. M 174.

c) Diamyl disulfide 0.49 g (3%).

B.p. 105-106° at 8-9 mm, d_4^{15} 0.9622, n_D^{15} 1.5047.

Found %: C 59.71; H 9.39; S 31.6. M 200; content of disulfide sulfur 95.0%. $(C_5H_{11})_2S_2$. Calculated %: C 58.25; H 10.68; S 31.07. M 206.

d) Diamyl tetrasulfide 2.14 g (18.7%).

B.p. 130-135° at 2 mm, d_4^{15} 1.0342, n_D^{15} 1.5410.

Found %: C 45.52; H 7.64; S 47.17. M 260. $(C_5H_{11})_2S_4$. Calculated %: C 44.44; H 8.15; S 47.40. M 270.

e) Crystalline sulfur 0.82 g (15.6%), m.p. 114°.

f) Residue-sulfur and polysulfides.

Reaction of H_2S_2 with cyclohexene. There was used 5.37 g of H_2S_2 in 80 ml of cyclohexene. There was isolated: a) H_2S 1.59 g (29.6%).

b) Dicyclohexyl monosulfide 2.36 g (7.75%).

B.p. 97° at 1 mm, d_4^{15} 0.9786, $n_D^{18.5}$ 1.5156.

Found %: C 72.51; H 11.08; S 16.69. M 195; content of monosulfide sulfur 98.9%. $(C_6H_{11})_2S$. Calculated %: C 72.72; H 11.11; S 16.16. M 198.

c) Dicyclohexyl disulfide 1.29 g (7.42%).

B.p. 125-130° at 1 mm, $n_D^{18.5}$ 1.5565.

Found %: C 59.19; H 9.65; S 30.47; content of disulfide sulfur 98.0%. $(C_6H_{11})_2S_2$. Calculated %: C 62.7; S 27.8. H 9.6.

Owing to low volatility, the higher sulfides were not isolated.

SUMMARY

1. It was shown that the thermal decomposition of hydrogen disulfide in hydrocarbon solvents proceeds through the stage of $\cdot SH$ radicals and $\cdot S_2H$ radicals.

2. It was established that the reactivity of α-olefins in respect to these radicals is much greater than that of β-olefins. The $\cdot SH$ radical does not participate in the reactions of cleavage of hydrogen from hydrocarbons.

3. The products of reaction of hydrogen disulfide with α- and β-pentenes and with cyclohexene were isolated and characterized and the mechanism of their formation was considered.

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ORIENTATION IN AROMATIC RING SUBSTITUTION

III. ISOMERIZATION OF DICHLOROBENZENES

A. A. Spryskov and Iu. G. Erykalov

When benzene is chlorinated, besides the mono-substituted chloride, a mixture of o- and p-dichlorobenzenes is formed at the ratio of 1 : 2.1 [1]; it also contains a small quantity of meta isomer [2]. In practice it is impossible to change the chlorine orientation successfully and obtain a different ratio of isomers. Orientation may be changed if halogenation is carried out at high temperatures, but the yields are very low. Thus at 450-600° one can get a disubstituted mixture containing 50-60% of meta isomer [3].

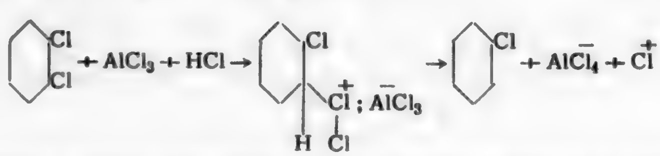
The ratio of isomers can also be changed through isomerization of the disubstituted halides. Thus, for example, when p-dichlorobenzene was heated with lead dioxide at 250-300°, conversion into meta isomer was observed [4]. A similar conversion takes place in the presence of aluminum chloride and hydrogen chloride [5], or in the presence of aluminum chloride alone at 175-250° [6]. The isomerization of o- and p-dichlorobenzenes in the presence of aluminum chloride was patented [7] as a method of preparing m-dichlorobenzene.

In several works the interconversions of 1- and 2-halo derivatives of naphthalene were described [8].

The purpose of the present investigation was to study the isomerization of dichlorobenzenes and to attain an equilibrium state between isomers at different conditions.

Starting with any dichlorobenzene isomer we attained a state of equilibrium between the isomers by heating with aluminum chloride at 160°. The equilibrium mixture contained 16% ortho, 30% para, and 54% of meta isomer. The rate of the isomerization process depended on the quantity of aluminum chloride; when it was increased from 0.1 to 1.5 moles per mole of dichlorobenzene the reaction rate increased, too. During isomerization disproportionation took place; we estimated that experiments in which temperature was kept at 160° during 50 hours yielded about 1.6% of monochlorobenzene. The amount of resin formed can reach 2.8%.

Experimental results provide grounds for the assumption that warming with aluminum chloride produces dehalogenation of dichlorobenzene with the formation of monochlorobenzene and liberation of chlorine. The latter chlorinates monochlorobenzene, forming a mixture of dichlorobenzenes. Dehalogenation proceeds through a donor — acceptor mechanism, as represented by equation



The hydrogen chloride formed in the system resulted from small quantities of moisture absorbed from the air by aluminum chloride. After the reaction tubes were heated, hydrogen chloride was detected.

Thus the chlorination reaction appears reversible in the presence of a catalyst. However, at low temperature the rate of the reverse reaction is so low that for all practical purposes halogenation proceeds irreversibly. With increase in temperature the rate of the reverse reaction (dehalogenation) increases, and isomerization reaction becomes possible; consequently a state of equilibrium can be achieved in the system.

EXPERIMENTAL

The p-dichlorobenzene used in this work had m.p. 53°. The m-dichlorobenzene (f.p. −25°) was obtained from m-nitroaniline through the Sandmeyer reaction. The o-dichlorobenzene (f.p. −17.8°) was made from o-chloroaniline.

Isomerization experiments were conducted in the following fashion. The three isomeric dichlorobenzenes were introduced separately into three tubes together with aluminum chloride. The sealed tubes were heated in a thermostat, and then their contents was poured out into water acidified with hydrochloric acid (in experiments where considerable resinification occurred, the mixture was filtered with suction). Dichlorobenzene was isolated in a separatory funnel, washed, dried with calcium chloride, and distilled under 12-15 mm pressure into a weighed receiver for the determination of freezing point. If the distilled product would not solidify at room temperature, a fixed quantity of pure para isomer would be added in order to raise the freezing point of the mixture. After freezing-point determination the mixture was nitrated, reduced, and brominated just as previously described [9] for a complete analysis of mixture.

Table 1 lists experimental results from tubes heated at 160°. The experiments showed that in about 50 hours the isomeric system reached a state close to equilibrium.

In experiments where the heating lasted 75 hours, the composition of the mixtures differed very little from that of the previous set. The course of the isomerization process shows that interconversion proceeds fast during the first 15-20 hours, and then slows down considerably.

TABLE 1

Isomerization of Dichlorobenzenes at 160° in the Presence of 0.27 Moles of $AlCl_3$ (20 wt. %).

Duration of heating hours	Isomer.	Composition of mixture after isomerization (in %)		
		ortho	para	meta
5	Ortho	60.6	9.8	29.6
	Para	0	74.4	25.6
	Meta	6.0	14.2	79.8
15	Ortho	28.0	24.4	47.6
	Para	3.1	60.0	36.9
	Meta	8.4	27.3	64.3
20	Ortho	24.4	25.6	50.0
	Para	4.8	47.0	48.2
	Meta	9.8	29.3	60.9
30	Ortho	20.1	27.6	52.3
	Para	10.0	33.5	56.5
	Meta	12.9	30.4	56.7
50	Ortho	16.8	29.2	54.0
	Para	14.6	30.7	54.7
	Meta	14.9	30.6	54.7
75	Ortho	18.6	28.9	52.5
	Para	17.3	29.6	53.1
	Meta	16.9	29.5	53.6

The results of these experiments permit us to establish the following composition of the equilibrium mixture: ortho isomer 16%, para isomer 30%, meta isomer 54%; this composition can be attained by starting from any one of the three isomers. In order to ascertain the stability of such a mixture we made an artificial mixture of 17.5% ortho, 30% para, and 52.5% meta isomers and heated it at 160° during 25 hours. We found the following composition after heating: 19% ortho, 28.9% para, and 52.1% meta isomers, i.e., the composition of mixture was practically unchanged.

A second set of isomerization experiments was conducted by heating at 120°. Experimental results (listed in Table 2) show that after heating for 375 hours we were still unable to attain a state close to equilibrium, irrespective of the isomer started with. The isomerization process proceeds much slower at 120° than at 160°.

A third set of experiments was conducted in order to study what effect the amount of catalyst has on the reaction rate. We heated o-dichlorobenzene at 160° during 5 hours with various quantities of aluminum chloride. Experimental results listed in Table 3 show that with increase in the quantity of aluminum chloride the isomerization rate increases rapidly at first, then slowly; finally, 1.5 and 2 moles of aluminum chloride show the same action.

TABLE 2

Isomerization of Dichlorobenzenes at 120° in the Presence of 0.27 moles of $AlCl_3$ (20 wt. %)

Duration of heating (in hours)	Isomer.	Composition of mixture after isomerization (in %)		
		ortho	para	meta
25	Ortho	77.4	4.2	18.4
	Para	2.1	96.4	1.5
	Meta	3.2	2.9	93.9
50	Ortho	71.7	6.4	21.9
	Para	0.5	93.7	5.8
	Meta	2.2	7.7	90.1
100	Ortho	55.6	11.9	32.5
	Para	0.7	90.7	8.6
	Meta	4.1	11.1	84.8
200	Ortho	33.0	17.6	49.4
	Para	1.5	81.0	17.5
	Meta	6.0	20.3	73.7
375	Ortho	25.5	22.7	51.8
	Para	5.4	45.7	48.9
	Meta	4.1	28.5	67.4

TABLE 3

The Dependence of o-Dichlorobenzene Isomerization Results on the Quantity of $AlCl_3$ used; Reaction Carried 5 hours at 160°

Moles of $AlCl_3$ taken from each mole of dichlorobenzene	Composition of mixture (in % of isomeric sum)			Remainder from the weight of dichlorobenzene taken (in %)
	ortho	para	meta	
0.1	75.3	5.4	19.3	0.4
0.25	56.1	11.9	32.0	0.5
0.5	37.4	21.0	41.6	0.6
1.0	23.2	25.4	51.4	1.7
1.5	14.0	28.2	57.8	2.3
2.0	14.3	28.2	57.5	2.7

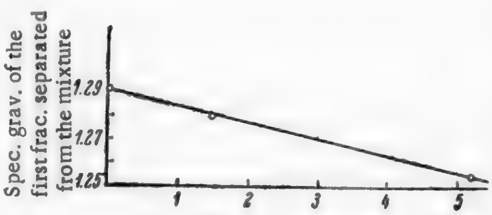
In the same set of experiments we determined the quantity of carbon-like substances formed during isomerization. Having poured the reaction mixture into water, we steam-distilled the dichlorobenzene in an apparatus [10] slightly improved by us. The residue, nonvolatile with steam, was filtered out and weighed. Results of these experiments, listed in the last column of Table 3, show that with increase in the amount of catalyst the quantity of residue increases too, not exceeding, however, 2.7% of the dichlorobenzene used. After heating the meta isomer with 20% aluminum chloride for 200 hours at 120° we found 0.3% of carbon-like substance; the ortho isomer produced 2.8% of this substance when heated 50 hours at 160°.

TABLE 4

Monochlorobenzene Contents, Following Isomerization of o-Dichlorobenzene at 160°

Moles of $AlCl_3$ taken for each mole of dichlorobenzene	Duration of isomerization (in hours)	Specific gravity of the first fraction	Monochlorobenzene contents (in %)
0.5	5	1.2865	0.6
0.5	5	1.2845	0.9
0.27	50	1.2794	1.6

We do not exclude the possibility that during isomerization of dichlorobenzene the disproportionation process goes through the formation of trichloro as well as monochlorobenzenes. Thus in the presence of aluminum bromide, bromobenzene undergoes very extensive disproportionation with the formation of benzene and polybromobenzenes [11]. In our experiments we estimated the degree of disproportionation of dichlorobenzene in the following manner. The vacuum-distilled mixture of dichlorobenzenes was fractionated into two parts. The specific gravity of the first fraction was determined in an Ostwald pycnometer; the amount was 1.4 ml out of 6-6.3 ml distilled off during 1-1.5 hours in a small fractionating column. Artificial mixtures of pure isomeric dichlorobenzenes and chlorobenzene were made up and fractionated. In the artificial mixtures the content of isomers was varied from 37 to 54% for the ortho, 14-21% for the para, and 29-42% for the meta. Large or small contents of individual isomers are hardly reflected at all in the specific gravity. The straight line constructed through three points in the figure represents the specific gravities of the first fractions separated from the artificial mixtures. We estimated the degree of disproportionation by comparing the specific gravity of the experimental first fraction with that of the artificial mixture on the straight line in the figure. The experimental results listed in Table 4 show that the monochlorobenzene content increases if duration of isomerization is increased. The degree of disproportionation was not large and even when the mixture was heated for 50 hours at 160° the monochlorobenzene contents did not exceed 1.6%.



SUMMARY

Isomerization of o-, m-, and p-dichlorobenzenes in the presence of aluminum chloride at 120 and 160° was studied. During 50 hours at 160° a composition close to that of equilibrium was attained; one could start from any isomer. The equilibrium mixture was composed of 16% ortho, 30% para, and 54% meta isomers. At 120° the isomerization proceeded considerably slower, and the equilibrium mixture was far from being attained.

Isomerization rate was raised when the amount of aluminum chloride increased from 0.1 to 1.5 moles per mole of dichlorobenzene.

During isomerization disproportionation of chlorine was detected. The maximum amount of monochlorobenzene constituted 1.6%. From 0.5 to 2.8% of carbonized residue was formed in the reaction mixture.

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THE STUDY OF SULFONATION REACTION

XLVII. THE STUDY OF CHLOROBENZENESULFONIC ACID HYDROLYSIS WITH THE USE OF RADIOACTIVE INDICATORS

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It is known that the rate of sulfonic acid hydrolysis depends on temperature, the nature and concentration of the mineral acid present, and on the concentration of the sulfonic acid itself [1]. Thus, when the sulfuric acid concentration in the reaction mixture is increased, the hydrolysis rate of sulfonic acid increases too. We showed [2] however, that when the sulfuric acid concentration was increased from 90 to 100% isomerization of m-benzenedisulfonic acid, which proceeds through hydrolysis, was slowed down. During investigation of 1,3,6-naphthalenetrisulfonic acid hydrolysis at 180° it was discovered that by increasing the sulfonic acid concentration to 87.6% one could increase also the quantity of desulfonated acid, but when concentration was further increased to 95.9% the quantity of desulfonated sulfonic acid diminished. However, the latter decrease is connected with the resulfonation of the hydrolyzed product; the rate of sulfonation increases rapidly with increase in the sulfuric acid concentration. The resulfonation interfered with the study of high sulfuric acid concentration effects on the hydrolysis rate of sulfonic acid, since hydrolysis reaction rates were estimated from the quantity of hydrolyzed products or from the increase in the amount of sulfuric acid found in the mixture.

In order to avoid these difficulties, we used sulfuric acid which was labeled with S^{35} isotope. If the chlorobenzenesulfonic acid, mixed with radioactive sulfuric acid, undergoes only hydrolysis when temperature is raised, then the remaining sulfonic acid will remain non-radioactive, and the amount hydrolyzed can be determined from the increase of sulfuric acid. If, however, with increase in sulfuric acid concentration sulfonation reaction begins to take place side by side with hydrolysis, then the chlorobenzenesulfonic acid will become radioactive.

In this manner an increase in the activity of sulfonic acid reflects increased rates of both processes; this can be used to study the effect of concentrated sulfuric acid on the rate of hydrolysis.

EXPERIMENTAL

In the hydrolysis experiments o-chlorobenzenesulfonic acid was used, because its hydrolysis product (chlorobenzene) is resulfonated with the formation of p-chlorobenzenesulfonic acid only [4], and the para isomer is much harder to hydrolyze than the ortho [5]. The para isomer on repeated hydrolysis changes through resulfonation back into an acid of the same activity. Thus the radioactive indicator method detects only the process in which ortho acid is changed into para.

Experimental mixtures were composed of o-chlorobenzenesulfonic acid and water at a molar ratio of 1 : 4.5 and varying quantities of anhydrous radioactive sulfuric acid (specific activity 0.15-0.28 in mCu/g) so as to obtain any desired concentration. The mixtures were placed in sealed test tubes and warmed in a thermostat. Samples of reaction mixtures were removed before and after heating, then titrated with 0.1 N alkali to determine the over-all acidity; decrease in acidity would indicate formation of disulfonic acids, while increase was used to calculate the amount of acid hydrolyzed. After heating we dissolved the mixture in water, boiled the solution and treated with excess barium carbonate; the solution was then cooled and the precipitate filtered out and washed. The filtrate and washings were made-up to 50 ml.

To measure the activity we poured the experimental solution on a mica window of a vertically-placed flat counter (type MST-17) in a hollow made of bolted plate-iron walls. A protective cover was placed on top. The thickness of the soultion layer should exceed the maximum range of S^{35} beta particles. Counting time was chosen so that the statistical error would not exceed ±2% (35-45 minutes). This measuring method was used by us in the 3rd series of experiments.

The 1st series of experiments was conducted by heating the reaction mixture during 10 hours at 150 ± 0.2° and with an experimental accuracy of ±5%. The experimental results are shown in Fig. 1. Ordinates in Curve 1 were calculated from the total increase in acidity of the mixture. When sulfuric acid concentration is increased the amount of hydrolyzed sulfonic acid increases, attains a maximum in 75% acid, and then diminishes to almost nothing in 87% sulfuric acid. Curve 2, obtained by measuring the activity of sulfonyl chloride isolated from the mixture, shows that in 66% sulfuric acid only hydrolysis takes place since the activity of sulfonic acid is zero. The ordinates of Curve 2 are expressed in terms of the relative specific activity of solution. As the concentration of sulfuric acid in the mixture was raised to 74-76%, the activity of sulfonic acid increased slowly at first and then very rapidly. Thus in about 75% sulfuric acid the resulfonation process starts growing rapidly. becomes observable and measurable. In 89% sulfuric acid the presence of disulfonic acids was detected as well as complete absence of hydrolysis products. At a point corresponding to A in the curve, a break was observed since the activity of disulfonic acid is considerably larger than that of monoacid. From the character of the curve section close to point A one can assume that the resulfonation reaction is slowed down and so is hydrolysis. It is possible that close to point A the hydrolysis reaction rate really decreases and the curve goes through a maximum.

We set up the 2nd series of experiments, in which the mixtures were heated at 126 ± 0.5° during 100 hours, with the purpose of detecting the maximum on the sulfonic acid activity curve and at the same time aiming to avoid disulfonation.

Curve 1 (Fig. 2) shows how the change in the specific molar activity of sulfonic acid depends on the concentration of sulfuric acid in solution; it represents the results of experiments carried out with an accuracy of 2-2.5%. Data from experiments in which disulfonation was absent are joined with the solid line.

Hydrolysis of o-Chlorobenzenesulfonic Acid (with Resulfonation at 119 ± 0.5° During 50 hours in the Presence of Sulfuric Acid and 4.55 Moles of Water per Mole of Sulfonic Acid

Concentration		Net counting rate after deduction of control (in counts/minute)	Specific molar activity (in counts/liter min·mmole).
of sulfuric acid (in %)	of meas. solution (in mmoles/liter)		
85.4 *	—	6.4 ± 1.6	—
85.4	44.1	511 ± 8	11.6 ± 0.2
86.2	37.7	612 ± 10	16.2 ± 0.3
87.1	26.6	569 ± 17	21.4 ± 0.6
87.5	23.0	494 ± 8	21.5 ± 0.3
88.5	20.5	497 ± 8	24.2 ± 0.4

*Control: the reaction mixture was not heated, but measured as described.

The last data were determined in 88% acid and therefore the results of this experiment are joined to the remaining ones by a dotted line. Thus the curve shows a maximum in degree of resulfonation which reflects the hydrolysis reaction rate.

The attempt to obtain a more precise maximum induced us to set up a 3rd series of experiments in which the mixture was heated during 50 hours at 119 ± 0.5°.

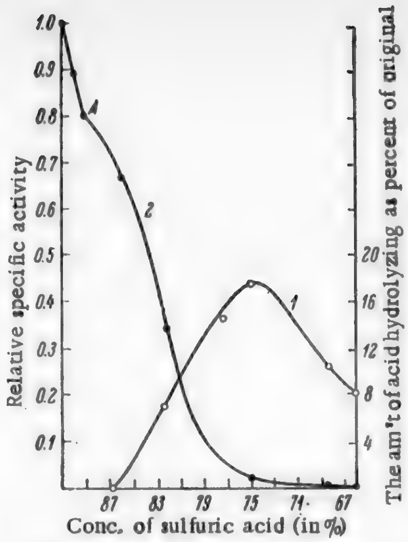

Fig. 1. Change in the relative hydrolysis reaction rate of o-chlorobenzenesulfonic acid in the presence of sulfuric acid at 150°. 1) The amount of hydrolyzed sulfonic acid found from the over-all increase in acidity of mixture; 2) relative specific activity of chloride separated from the mixture.

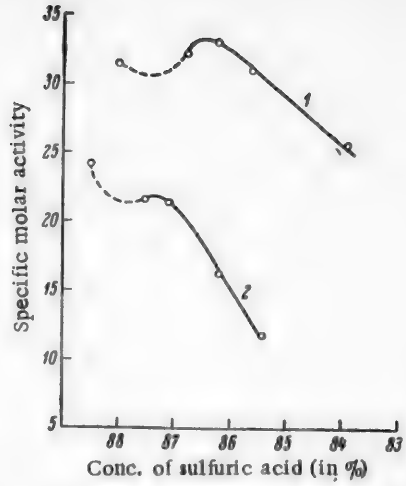

Fig. 2. Change in the relative hydrolysis reaction rate of o-acid at 119 and 126°. 1) Change in specific molar activity of sulfonic acid in reaction mixture after 100 hours at 126°; 2) change in specific molar activity of sulfonic acid in reaction mixture after 50 hours at 119°.

The experimental results, listed in the table and shown as Curve 2 in Fig. 2, indicate that in 87.5% sulfuric acid no increase in sulfonic acid activity takes place as compared to the preceding run in 87.1% acid.

On Curve 2 (Fig. 2) a sharp change in the curve direction occurs, but we were still unable to obtain a precise maximum since in the subsequent run (in 88.5% sulfuric acid) the presence of disulfonic acids became noticeable again.

The correction for isotope dilution was computed in experiments of 2nd and 3rd series but turned out very small and therefore was not included in the results. Approximate calculations give the degree of resulfonation, i.e. for the hydrolyzed and resulfonated part of the whole acid, in the range of 42-54% for the 2nd set of experiments, and 16-54% for the 3rd.

DISCUSSION OF RESULTS

On the basis of our experimental results we can assume that the rate of the sulfonic acid hydrolysis increases with the increase in sulfuric acid concentration, attains a maximum and then decreases. The hydrolysis rate maximum for o-chlorobenzenesulfonic acid was observed at a sulfuric acid concentration of approximately 87% in the 120-150° temperature range.

Earlier [2] we have recorded an increase in the isomerization rate of m-benzenedisulfonic acid when the concentration of sulfuric acid was decreased from 100 to 90%. The equilibrium constant for the reaction $H_2SO_4 + H_2O \rightleftarrows H_3O^+ + HSO_4^-$ in concentrated sulfuric acid solutions was calculated:

$$K = \frac{[H_3O^+][HSO_4^-]}{[H_2O]} = 1.2 \text{ mole/kg.}$$

With the usual assumptions we calculated the H_3O^+ concentration in sulfuric acid containing from 5 to 30% water by introducing the molar concentration (10.2) of sulfuric acid into the equation; we found out that when the sulfuric acid is diluted the H_3O^+ concentration has a maximum in 80% sulfuric acid. Taking into consideration the assumptions made, the various temperatures of hydrolysis and of experiments run to calculate the equilibrium in sulfuric acid, and also the presence of sulfonic acid in sulfuric, we can presume that there

exists in sulfuric acid a well known correspondence between the type of H_3O^+ concentration curve and the rate of sulfonic acid hydrolysis [5], according to which the hydrolysis reaction rate depends on the concentration of the intermediate complex whose concentration in turn depends on that of H_3O^+ ion.

SUMMARY

o-Chlorobenzenesulfonic acid was hydrolyzed at 119, 126, and 150° in the presence of sulfuric acid of varying concentrations. Up to 86-87% sulfuric acid concentrations the hydrolysis reaction rate increases, then the increase stops and even a slight decrease begins. Starting with 88% sulfuric acid the disulfonation reaction prevents us from obtaining a well defined maximum on the curve of reaction rate vs. sulfuric acid concentration.

The investigation was conducted radiometrically; we used sulfuric acid labeled with S^{35}.

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MECHANISM OF α-TETRALOXIME CONVERSION INTO α-NAPHTHYLAMINE

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The conversion of cyclic ketoximes possessing one double bond in a six-membered ring or a heterocyclic sulfur in a five-membered ring into aromatic amines has been known for a fairly long time and has been suitably applied to a large number of compounds. The conditions described in the literature for effecting this conversion are extremely diverse. Thus carvenoxime hydrochloride changes into carvacrylamine hydrochloride on dry distillation [1]; 1,2,3,4-tetrahydroquinoloxime-4 gives 4 aminoquinoline when warmed with activated charcoal in vacuo [2]; isophoroxime changes into 3,4,5-trimethylaniline when heated to 170° with 20% hydrochloric acid [3] (however, compare [4]); thujoxime gives carvacrylamine when heated in 50% alcoholic sulfuric acid solution [5]; 1-phenyltetraloxime-2 changes into 1-phenylnaphthylamine-2 hydrochloride when heated with hydrogen chloride in absolute alcohol [6]. With a number of 3-ketotetrahydrothiophene derivatives the conversion into the corresponding 3-aminothiophenes takes place when hydrogen chloride is introduced into an ether solution of the oxime [7]. Oximes of substituted cyclohexenones change into corresponding N-acetanilides when warmed with acetyl chloride [3], acetic anhydride [3, 8], acetic anhydride and sodium acetate [9], and also on interaction with acetyl chloride in acetic anhydride in the presence of pyridine [4] (compare [10]). Schroeter and co-workers [11] showed that oximes of α-tetralone and of its derivatives (except 8-substituted) change into corresponding α-naphthylamines on treatment with "Beckmann's mixture" (solution of acetic anhydride in glacial acetic acid saturated with hydrogen chloride) at 100° (see also [7, 12]). The sulfate of α-tetraloxime changes into α-naphthylamine under the action of hydrogen chloride in dioxane [13].

The mechanism by which ketoximes are converted into aromatic amines has not been elucidated until now.

We investigated the conversion of α-tetraloxime into α-naphthylamine under conditions described by Shroeter and co-workers [11], i.e., by heating it at 100° with 1.3 moles of acetic anhydride in glacial acetic acid in the presence of hydrogen chloride. The reaction mass obtained in this manner yielded 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I, approx. 2.0%) and 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II, 8.6%) besides previously [11] detected α-naphthylamine hydrochloride (31.0%) and N-acetyl-α-naphthylamine (3.3%). (I) was identified in the form of oxime which was prepared by the method described for 2-bromo-1-keto-1,2,3,4,-tetrahydronaphthalene [14].

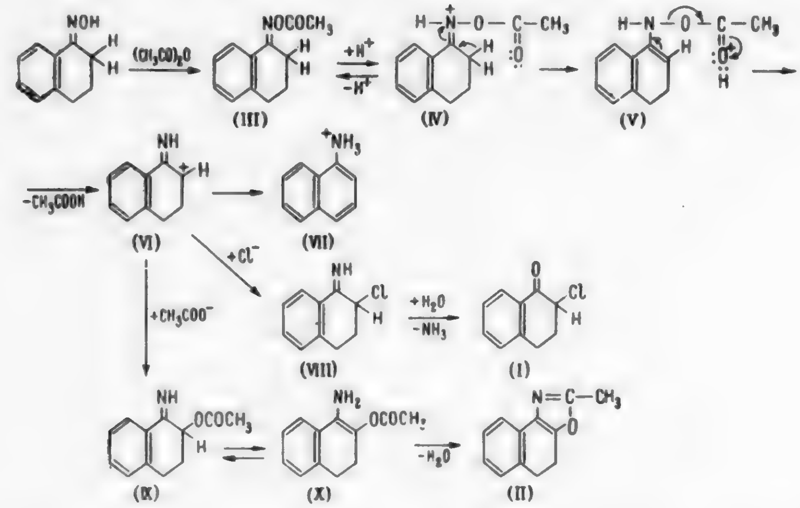
The structure of the previously undescribed compound (II) was determined by dehydrogenation with diphenyldisulfide (see [15]) into 2-methyl-(naphtho-1',2':4,5-oxazole) (yield 87.5%, identified as picrate and methiodide), and through synthesis (yield 12.7%) from 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (see [16] for method of obtaining oxazoles).

Since one of the methods used to obtain oxazoles consists of heating α-haloketones with ammonium formate in formic acid [17, then one could presume that during conversion of α-tetraloxime into α-naphthylamine, compound (II) results from the interaction between compound (I), acetic acid, and ammonium chloride; ammonium chloride was detected among reaction products (16.4% yield, based on α-tetraloxime). We heated (I) with ammonium chloride (and also with acetamide) in acetic acid in a stream of hydrogen chloride but were unable to obtain (II).

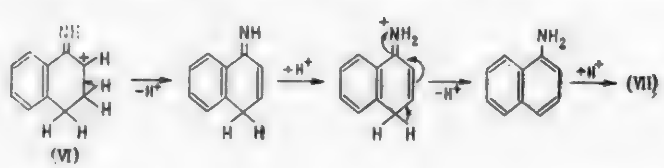
Compound (II) in its turn, could not be an intermediate product in the formation of α-naphthylamine since it does not undergo any change when heated in acetic acid with hydrogen chloride.

Determination of the nature of side products will permit a better understanding of the mechanism by which α-tetraloxime is converted into α-naphthylamine. The first reaction product is O-acetyl derivative of α-tetraloxime (III),* which precipitates in the form of white crystals when acetic anhydride is added to the solution of oxime in glacial acetic acid. Since acetic anhydride is not required in further conversion of O-acetyl derivative (III) into α-naphthylamine (see experimental part), then it follows that the function of acetic anhydride consists of oxime acetylation.

The O-acetyl derivative of α-tetraloxime does not change when heated at 100° in glacial acetic acid. But under the same conditions it will change to α-naphthylamine (and side products) if hydrogen chloride is present. The mechanism of this conversion can be described by the following scheme:



The attack of a proton on the nitrogen in the acetyl derivative of the oxime (III) and the subsequent electron displacement result in a transfer of hydrogen (in the form of a proton) from a ring carbon to the oxygen in the acetyl group, as shown by structures (IV) and (V); after this, acetic acid is split-out and a carbonium ion is formed (VI). As a result of proton transfer, the last one isomerizes into naphthylammonium ion (VII),



while with Cl^- and CH_3COO^- anions it changes into 2-chloro- and 2-acetoxy-1-imino-1,2,3,4-tetrahydronaphthalene, respectively (VIII and IX). The tautomeric form of (I) – 1-amino-2-acetoxy-3,4-dihydronaphthalene (X), changes into (II) by splitting out a molecule of water. Formation of the last one should proceed fairly easily, since it is known that the aromatic analog of (X) – 1-amino-2-acetoxynaphthalene – cannot be obtained since it readily converts into the corresponding oxazole [18]. In water (VIII) hydrolyzes to (I).

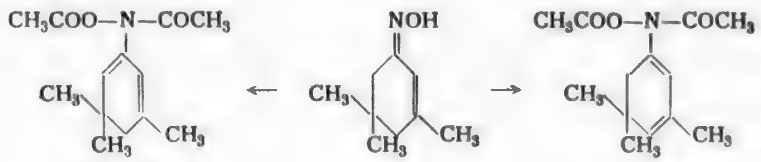
It is hardly possible under these conditions to split out hydrogen chloride from (VIII) and form α-naphthylamine, for the 2-halo-1-keto-1,2,3,4-tetrahydronaphthalenes are characterized by a comparatively small tendency to dehydrohalogenate [19].

*Schroeter and co-workers [11] assumed that the reaction starts with addition of hydrogen chloride to the oxime or to its acetyl derivative.

The proton donor in the examined reaction is hydrogen chloride; this is obvious from comparison of following data. The dissociation constant of 100% acetic acid is $\sim 1.43 \times 10^{-14}$ at 25°*, while that of hydrogen chloride in 100% acetic acid equals 5.1×10^{-10} [21], i.e. 3.5×10^{4} times larger. This explains why in the absence of hydrogen chloride the acetyl derivative of the oxime does not change into α-naphthylamine.

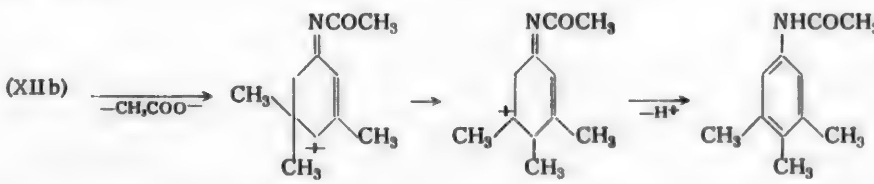
It has been noted [11] that the p-toluenesulfonyl derivative of α-tetraloxime undergoes normal Beckmann rearrangement under the same conditions that lead to the conversion of oxime acetate into α-naphthylamine. From the point of view of the proposed mechanism, this can be explained by a decrease in the basicity of the oxime nitrogen (low to begin with) when the acetyl group is replaced with a more electrophilic p-toluenesulfonyl radical; as a result, the ability of a proton to attack the oxime nitrogen is reduced.

One should note that in the opinion of investigators [4] the conversion of isophoroxime (XI) into a mixture of N-acetyl derivatives of 2,3,5- and 3,4,5-trimethylaniline under the action of acetyl chloride and pyridine in acetic anhydride evidently proceeds also through the formation of a carbonium ion intermediate. These authors put forward a working hypothesis that the reaction begins with the formation of hypothetical O,N-diacetyl derivatives of isophoroxime (XII a,b)



(XIIa) (XI) (XIIb)

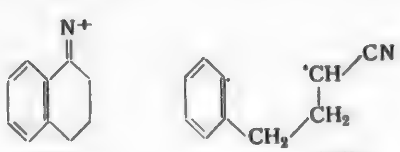
and proceeds as below,



Compound (XII a) changes into N-acetyl-2,3,5-trimethylaniline in a similar fashion.

Migration of the methyl group, observed in this case, is a strong argument in favor of a carbonium ion intermediate. But the formation of O,N-diacetyl derivatives of the oxime seems questionable to us. It is natural to assume that the conversion in this case proceeds through a monoacetyl oxime derivative with the formation of amine, which then undergoes acetylation.

Hardy and co-workers [12] have recently repeated the conversion of 7-nitrotetraloxime-1- into 7-nitronaphthylamine-1 (described by Schroeter [11]) and came out with the hypothesis that aromatization proceeds through the formation of an intermediate ion (XIII) or a biradical (XIV).

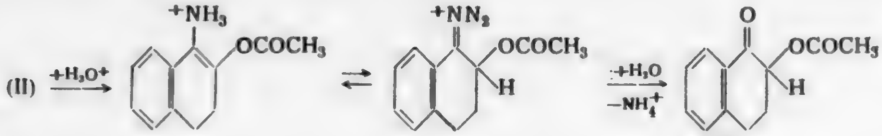


(XIII) (XIV)

*Calculated from the autoprotolysis constant $[CH_3COOH_2^+] \cdot [CH_3COO^-] = 2.5 \cdot 10^{-13}$ [20].

However, neither hypothesis makes it possible to explain the formation of the reaction products we isolated (not to mention other serious shortcomings in the scheme of Hardy and co-workers).

We obtained some interesting results while studying the reactions of 2-methyl-3',4'-dihydronaphtho-1', 2':4,5-oxazole (II). We found out that when it was boiled with hydrochloric acid, β-naphthol formed readily (91% yield). This unexpected conversion was explained as follows: acidic cleavage of (II) forms 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene (XV) as a first step.



(XV)

The conversion of the latter into β-naphthol, caused by boiling it with hydrochloric acid, has already been described [22].

If the acid cleavage of (II) is carried out at room temperature with the use of dilute hydrochloric acid in the presence of 2,4-dinitrophenylhydrazine hydrochloride, then the reaction stops at the ketone (XV) stage; the ketone precipitates as 2,4-dinitrophenylhydrazone out of reaction mixture. In order to identify the product obtained, we prepared a 2,4-dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene by starting with 2,4-dinitrophenylhydrazone of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene [23].

The cleavage of the N−C bond in oxazole (II) is somewhat unexpected since acids usually cleave the O−C in oxazoles. In particular, one should have expected (see [16]) to form the 2,4-dinitrophenylhydrazone of 1-acetamide-2-keto-1,2,3,4-tetrahydronaphthalene by the action of dilute hydrochloric acid on oxazole (II) in the presence of 2,4-dinitrophenylhydrazine.

EXPERIMENTAL

α-Tetralone was obtained through cyclization of γ-phenylbutyrylchloride [24]; the yield was 92.5% b.p. 110.5-112.5° at 5 mm, n_D^{20} 1.5691. According to lit. data [25]; b.p. 105° at 3 mm, n_D^{20} 1.5691, 1.5693.

Oxime: yield 94%, m.p. 100.5-101.5° (from aqueous methanol). According to lit. data [25]: m.p. 102.5-103.5°.

Elucidation of the acetic anhydride and hydrochloric acid role in the conversion of α-tetraloxime into α-naphthylamine. Experiment 1. We added 2.25 ml of acetic anhydride to a solution containing 3.0 g of α-tetraloxime in 19.0 ml of 99.8% acetic acid at room temperature. In about 1-1.5 minutes a white O-acetyl derivative of the oxime (III) precipitated. The yield was 3.7 g (97.5%), m.p. 144.0-144.5°. According to lit. data [11]: m.p. 148°. Experiment 2. We dissolved 1.5 g of the oxime acetyl derivative in 7.5 ml of hot 99.8% acetic acid and kept the solution for 10 min in a 110° bath; at the same time hydrogen chloride was bubbled through it. When the solution cooled, slightly greyish crystalline α-naphthylamine precipitated (see below for identification); the yield was 0.48 g (36.2%). Experiment 3. After mixing 2.5 g of α-tetraloxime acetyl derivative, 0.34 ml of acetic anhydride, and 12.5 ml of 99.8% acetic acid we heated them for 1 hour in a 110° bath. We isolated 1.80 g (72%) of the starting material, m.p. 144-145°, from the reaction mixture diluted with water.

Investigation of the α-tetraloxime conversion products. Experiment 4. The reaction was carried out in a four-necked flask provided with a reflux condenser, a thermometer, a stirrer, and a tube to introduce hydrogen chloride under the liquid surface.

To a 50 g solution of α-tetraloxime in 310 ml of 99.6% acetic acid 37.5 ml of acetic anhydride was added. After 1-1.5 minutes the whole mixture solidified due to the formation of the acetyl derivative of oxime (III). When after 45 minutes the bath temperature was raised to 100° the acetyl derivative went into solution which gradually acquired a violet-red color. Having turned the stream of hydrogen chloride on (50-70 ml/min.), we maintained the reaction mixture at 100° for 2 hours. During this time the reaction mixture gradually darkened, and eventually became almost black. The grey crystalline precipitate of α-naphthylamine hydrochloride, which formed when the solution was cooled, was filtered out and washed with 100 ml of glacial

acetic acid. The weight of precipitate was 14.90 g. When we benzoylated 0.50 g of it in the usual manner, we obtained 0.67 g (97.5%) of the benzoyl derivative of α-naphthylamine, m.p. 159-160° after recrystallization from ethyl alcohol. According to lit. data [26]: m.p. 161°.

After removing α-naphthylamine hydrochloride we distilled off in vacuo (bath temperature 80°) the acetic acid from the filtrate. We triturated the resinous residue (a) with 50 ml of chloroform; the precipitate that formed was filtered out and washed with 25 ml of chloroform. The grey crystalline precipitate weighed 4.0 g. From 0.50 g of the precipitate we obtained on benzoylation 0.21 g (30.5%) of N-benzoyl-α-naphthylamine, m.p. 151-153°. Besides this, the precipitate contained ammonium chloride (68% by weight of precipitate) and did not contain any hydroxylamine hydrochloride (qualitative test with iodine and sulfanilic acid). The ammonium chloride content was determined in the usual fashion by distilling off the amine from an alkaline solution (diazotization was used to determine the amount of co-distilled α-naphthylamine). The ammonium chloride yield was 2.72 g of 16.4% if computed from α-tetraloxime.

The chloroform filtrate was extracted with 0.5 N hydrochloric acid solution (10 portions of 30 ml each). The hydrochloric solution was washed with chloroform and ether, treated with solid sodium carbonate until it became alkaline, and extracted with ether. When hydrogen chloride (dried over anhydrous sodium sulfate) was passed through the ether solution a crystalline precipitate of α-naphthylamine hydrochloride formed; the weight was 1.1 g. Benzoylating 0.22 g of it, we obtained 0.27 g (89%) of N-benzoyl-α-naphthylamine, m.p. 159.5-160.5°; after recrystallization from ethyl alcohol. Thus the over-all yield of α-naphthylamine was ~17.2 g (31.0%).

After extraction with hydrochloric acid the chloroform solution was washed with 10% sodium carbonate solution and then with water. The chloroform was distilled off in vacuum (bath temperature 50°) and the residue steam-distilled. A black tarry residue (b) remained in the flask. The oil that distilled off with 2 liters of distillate was extracted with ether. When hydrogen chloride (dried over anhydrous sodium sulfate) was passed into the ether solution of slightly greyish precipitate (v) formed; it weighed 9.90 g. The precipitate obtained contained ~60% of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole hydrochloride (~8.6% yield) and practically no α-naphthylamine hydrochloride.

The oxazole hydrochloride contents in the precipitate was determined from the picrate yield (0.66 g of picrate, m.p. 143.5-144.5, were obtained from 0.56 g of precipitate) and also from the yield of β-naphthol formed when precipitate (v) was boiled with dilute hydrochloric acid (1 : 1) (from 1.02 g of precipitate (v) 0.34 g of β-naphthol was obtained). We were not able to separate the pure oxazole by fractionating the base obtained from precipitate (v). (Isolation of oxazole in a pure form is described in experiment 5).

Having removed precipitate (v) we washed the ether filtrate with 5% sodium bicarbonate solution and water, dried with sodium sulfate, and concentrated by evaporation. Fractional distillation of the residue (in a Claisen flask with a 7 cm fractionating column) gave the following fractions: 1st b.p. 125-132° at 14 mm; weight 4.64 g; 2nd. b.p. 132-152° at 14 mm, weight 1.13 g; 3rd b.p. 152-162° at 14 mm, weight 2.22 g; residue 1.5 g of a brown viscous oil.

1st Fraction – colorless mobile liquid which, as the boiling point would indicate, must be α-tetralone The literature [25] gives b.p. 134° (at 15 mm) for α-tetralone. When we boiled (30 minutes) 1.45 g of the 1st fraction with 1.4 g of hydroxylamine hydrochloride and 1.5 g of potassium carbonate in a mixture of 9 ml methanol and 6 ml water, we obtained 1.43 g (89.3%) of α-tetraloxime which had a m.p. 101-102° after recrystallization from dilute methanol. This sample if mixed with known α-tetraloxime produced no melting point depression. The yield of α-tetralone was 10.2%.

3rd Fraction – colorless viscous oil containing halogen (Beilstein's test). The oil was soluble in ether and in methanol but not in petroleum ether. Skin irritating action as well as boiling point would permit us to assume that the 3rd fraction contains 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I). The literature reports [27] b.p. 157-160° (at 14 mm) for this ketone. To a 1.25 g solution of the 3rd fraction in 15 ml of methanol we added 1.25 g of hydroxylamine hydrochloride dissolved in 2 ml of water; the clear solution was left standing 24 hours at room temperature. After this we diluted it with 20 ml of water and extracted the oil that separated-out, three times with 3 ml portions of chloroform. When hydrogen chloride was bubbled through the chloroform solution a white crystalline precipitate of oxime hydrochloride formed; the yield was 0.78 g m.p. 124-130° (in a sealed capillary). To convert the hydrochloride into free oxime we dissolved it in 6 ml of methanol

and diluted with 6 ml of water. A white crystalline precipitate formed; its yield was 0.36 g m.p. 105-116°. Recrystallization from petroleum ether (b.p. 80-100°) gave white needles, m.p. 117.5-118.5°.

Found %: N 7.20, 7.34. $C_{10}H_{10}ONCl$. Calculated %: N 7.16.

A sample of it mixed with known oxime of 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (see below) did not lower the melting point.

Thus the third fraction contained 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (~50% by weight); its yield was 2.0%. We extracted 1.90 g (3.3%) of N-acetyl-α-naphthylamine from the tarry residue (b) using boiling water (10 times with 50 ml samples). The N-acetyl-α-naphthylamine m.p. 158-159° (recrystallized from methanol). According to literature [26]; m.p. 160°.

A sample mixed with known N-acetyl-α-naphthylamine did not lower the melting point.

After the remainder of residue (b) was made alkaline, a black brittle resin remained which was soluble in chloroform but not in hot methanol or glacial acetic acid – the yield, 11.2 g.

Experiment 5. It was similar to experiment 4. The residue (a) was treated with 100 ml of ether and 200 ml of water. After shaking for 15 minutes we filtered it, separated the ether layer, and extracted the aqueous layer with ether (twice with 50 ml samples). The ether extracts were dried over anhydrous sodium sulfate, and then hydrogen chloride was bubbled through producing a precipitate (g) of 2-methyl-3',4'-dihydronaphtho-1', 2', : 4,5-oxazole; its yield was 8.9 g (13%). When placed in water the hydrochloride hydrolyzed producing an oily base. The hydrochloride was triturated with water, the precipitate produced extracted with ether, and vacuum-distilled in a flask outfitted with a Claisen head and an 8 cm fractionating column. We obtained a colorless liquid posessing a peculiarly pleasant odor; its yield was 5.5 g (9.6%).

Analysis and molar refractions correspond to those calculated for 2-methyl-3',4'-dihydronaphtho-1',2': 4,5-oxazole (II):

B.p. 104° at 0.5 mm, d_4^{16} 1.1855, n_D^{16} 1.5948, MR_D 53.07; calculated 53.47.

Found %: C 77.40, 77.30; H 5.97, 6.12; N 7.57, 7.69. $C_{12}H_{11}ON$. Calculated %: C 77.80; H 5.99; N 7.56.

The picrate of oxazole (II) was made from 0.245 g of oxazole and 0.303 g of picric acid in 6 ml of absolute ethyl alcohol; the yield was 0.485 g (88.5%). Recrystallized from absolute ethyl alcohol it gave yellow needles, m.p. 145.5-146.0°.

Found %: C 52.05, 52.20; H 3.57, 3.68; N 13.35, 13.43. $C_{18}H_{14}O_8N_4$. Calculated %: C 52.18; H 3.41; N 13.52.

Methyl iodide derivative of oxazole (II). We heated 0.13 g. of methyl iodide with 0.29 g of oxazole (II) in a sealed glass ampule for 18 hours in a 115-125° bath. The precipitate obtained was transferred to a filter paper and washed with ether and acetone. We obtained small colorless needles, m.p. 210.0-211.5° (it remained the same after recrystallization from absolute ethyl alcohol); the yield was 0.43 g (84%).

Found %: C 47.91, 48.02; H 4.40, 4.51. $C_{13}H_{14}ONI$. Calculated %: C 47.72; H 4.31.

A sample of this derivative when mixed with some 2-methyl-(naphtho-1',2': 4,5-oxazole) methiodide (m.p. 210.1-211.5°, see below) melted at 202-203°.

Hydrochloride of oxazole (II) was made by bubbling hydrogen chloride through an ether solution of the b base; its m.p. 222-224° (in a sealed capillary, introduced at 180°). A substance with the same melting point was obtained when hydrochloride (g) was recrystallized from acetone (thin needles).

Found %: ionizable Cl 15.9, 160. $C_{12}H_{12}ONCl$. Calculated %: Cl 15.99.

The hydrochloride was soluble in chloroform and glacial acetic acid, but not in benzene and ether.

Dehydrogenation of 2-methyl-3',4'-dihydronaphtho-1',2': 4,5-oxazole (II) into 2-methyl-(naphtho-1', 2': 4,5-oxazole). We heated 0.30 g of 2-3',4'-dihydronaphtho-1',2': 4,5-oxazole with 0.53 g of diphenyldisulfide for 2 hours in a sealed glass tube at 260-265°. The reaction mixture was a yellow liquid with a strong odor of

thiophenol; it was dissolved in 8 ml of ether through which hydrogen chloride was allowed to bubble. The precipitate that formed was filtered out and washed with ether until the odor of thiophenol disappeared. We obtained 0.31 g (87.3%) of 2-methyl(naphtho-1',2':4,5-oxazole) hydrochloride (XIV), m. p. 164-174° (in a sealed capillary). According to lit. data [28]: m.p. 177°.

We converted 0.13 g of the hydrochloride (XIV) into the free base: treatment of the base with 0.14 g of picric acid in 4 ml of absolute ethyl alcohol produced the picrate of 2-methyl-(naphtho-1',2':4,5-oxazole), the yield of which was 0.204 g (83.8%). Recrystallization from absolute ethyl alcohol gave yellow needles, m.p. 148.5-149.5°. A sample of it mixed with 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole picrate melted at 135-137°. A sample mixed with known 2-methyl- naphtho- 1',2':4,5-oxazole) picrate (see below) did not lower the melting point.

Found %: N 13.76, 13.86; $C_{18}H_{12}O_8N_4$. Calculated %: N 13.59.

The free base obtained from 58 mg of hydrochloride (XIV) and 0.1 ml of methyl iodide were heated in a sealed glass tube during 15.5 hours in a bath at 115-125°. This yielded 40 mg (46.5%) of 2-methyl-(naphtho-1'2':4,5-oxazole) methiodide. The m.p. was 205-206° after recrystallization from absolute ethyl alcohol (purification is difficult due to the instability of the product [29]). A sample mixed with known 2-methyl-(naphtho-1',2':4,5-oxazole) methiodide (see below) did not lower the melting point.

A mixture containing 75 mg of hydrochloride (XIV), 1.5 ml of ethyl alcohol, and 0.5 ml of 12% hydrochloric acid was boiled with refluxing for 10 minutes. The resulting solution was evaporated down to 1 ml and diluted with 5 ml of water. A white precipitate was filtered out, washed with 12% hydrochloric acid solution, and dried out; the yield was 35 mg. After recrystallization from dilute methyl alcohol the m.p. was 228.5-230.0°. A sample of it when mixed with some 1-acetaminonaphthol-2 (m.p. 235-236°) produced no melting pount depression. According to lit. data [28]; m.p. 235°.

<u>The action of acids on 2-methyl-3',4'-dihydronaphto-1',2':4,5-oxazole (II).</u> A solution of 208.4 mg of oxazole (II) in 5 ml of hot concentrated hydrochloric acid was boiled for 2 hours with refluxing. When the solution was cooled a pink precipitate formed which was extracted with ether. Evaporation of ether yielded 148.0 mg (91.0%) of β-naphthol, m.p. 110-111°. The β-naphthol that formed did not produce coloration with p-toluenediazonium chloride in acetic acid [30]; this would indicate the absence of any α-naphthol in the sample. After reprecipitation from an alkaline solution and one recrystallization from water, the m.p. 120.0-121.0°. When mixed with a known sample of β-naphthol it did not lower the melting point. Having removed the β-naphthol we determined the amount of ammonia present in the hydrochloric acid solution; the quantity was 91.5% of theoretical.

Boiling of oxazole (II) with dilute hydrochloric acid (1 : 1) leads to the same results.

Oxazole (II) does not undergo any change when heated in glacial acetic acid saturated with hydrogen chloride. After heating it for 4 hours at 110-115° we recovered 87.5% of the starting material. No β-naphthol was detected.

<u>Interaction of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II) with hydrochloric acid and 2,4-dinitrophenylhydrazine.</u> A solution containing 0.72 g of 2,4-dinitrophenylhydrazine in 144 ml of 2 N hydrochloric acid was added to 0.72 g of oxazole (II) hydrochloride dissolved in 14.4 ml of 2 N hydrochloric acid and 50 ml of water. After 2 months an orange precipitate formed; yield 0.26 g, m.p. 140-150°. Two recrystallizations from ethyl acetate gave red crystals, m.p. 185-186°. A sample mixed with 2,4-dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene (see below) did not depress the melting point.

Found %: N 14.64, 14.82. $C_{18}H_{16}O_6N_4$. Calculated %: N 14.58.

<u>The action of potassium hydroxide on oxazole (II).</u> We boiled 134.5 mg of oxazole for 3 hrs. in a 5 ml of 30% potassium hydroxide solution. We recovered 84% of the starting material from the reaction mixture; it was isolated as hydrochloride, m.p. 222-224°. We were unable to detect any β-naphthol.

<u>Examination of the possibility to form oxazole (II) from (I) under the reaction conditions.</u> A mixture containing 1.0 g of (I), 0.296 g of ammonium chloride, and 6 ml of 99.5% acetic acid was kept in a 100° bath for 2 hours with hydrogen chloride bubbling through it (18 ml/min). The acetic acid was distilled off in vacuo,

the residue treated with 10% sodium carbonate, and extracted with ether. No precipitate formed when hydrogen chloride was passed through the ether solution which had been dried over anhydrous sodium sulfate.

Nor was any oxazole (II) detected among reaction products when equimolar quantities of (I) and acetamide in acetic acid were treated in the above described fashion.

The preparation of 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene (I) and its oxime. We obtained (I) by chlorinating α-tetralone [32]. The unpurified product melted at 38-41°; according to lit. data [32] for the pure product: m.p. 44-45.5°.

We dissolved 0.60 g of the prepared product and 0.60 g of hydroxylamine hydrochloride in a 9 ml methanol – 0.7 ml water mixture and left the resulting clear solution at room temperature for 24 hours. White oxime precipitated when the solution was cooled to 0° and diluted with 25 ml of cold water; the yield was 0.59 g (91.0%), m.p. 104-111°. After two-fold recrystallization from petroleum ether (60-80° fraction) we obtained tiny white needles, m.p. 120.0-120.5°.

The preparation of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole (II). Using a condenser outfitted with a calcium chloride tube we refluxed 2 g of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (obtained through bromination of α-tetralone [33]; yield 82.5%, m.p. 37-39°) with 1.2 g of acetamide in a 140° bath for 3 hours. The reaction mixture was shaken up with 10 ml of 10% sodium carbonate and 5 ml of benzene. The benzene layer was separated, washed with water, and dried over anhydrous sodium sulfate. When hydrogen chloride was bubbled through the benzene solution, 0.25 g (12.7%) of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole hydrochloride was formed.

The hydrochloride was converted into free base and made into picrate; after recrystallization from absolute ethyl alcohol the m.p. 144.5-145°. When a sample of it was mixed with some picrate of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole obtained from conversion of α-tetraloxime, no melting point depression was observed.

2-Methyl-(naphtho-1',2':4,5-oxazole) was prepared from 1-aminonaphthol-2 hydrochloride [29]; the yield was 50%, b.p. 161° at 15 mm; according to lit. data [28]: b.p. 158° at 14 mm.

Methiodide, the yield was 41.3%, m.p. 210.5-211.5°; according to lit data [29]: m.p. 212-213°.

Picrate, the yield was 94.5%, m.p. 148.3-149.5°.

2,4-Dinitrophenylhydrazone of 2-acetoxy-1-keto-1,2,3,4-tetrahydronaphthalene was made by starting with 2,4-dinitrophenylhydrazone of 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene (see [19]; 70% yield, m.p. 180.5-181.5°) and boiling it with anhydrous ethyl acetate (10% excess) for 20 minutes in glacial acetic acid. The yield was 90.8%. Recrystallization from ethyl acetate gave orange-red prisms, m.p. 185-186°; according to lit. data [23]: m.p. 186-187°.

SUMMARY

1. When α-tetraloxime was heated with acetic anhydride in glacial acetic acid, in the presence of hydrogen chloride, the following were formed: α-naphthylamine, N-acetyl-α-naphthylamine, α-tetralone, 2-chloro-1-keto-1,2,3,4-tetrahydronaphthalene, and 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole.

2. The structure of 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole was determined by dehydrogenation with diphenyldisulfide into 2-methyl-(naphtho-1',2':4,5-oxazole) and by synthesis from 2-bromo-1-keto-1,2,3,4-tetrahydronaphthalene and acetamide.

When boiled with hydrochloric acid, 2-methyl-3',4'-dihydronaphtho-1',2':4,5-oxazole was converted into β-naphthol.

3. A mechanism which explains the formation of all the isolated products is proposed for the conversion of α-tetraloxime.

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THE PROBLEM OF THE REDUCTION OF 1-METHYL-1-CYCLOHEXENE OXIDE

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In 1952 Mousseron and co-workers [1] published the results of the reduction of 1-methyl-1-cyclohexene oxide with lithium aluminum hydride. The only product of this reaction was the tertiary alcohol, 1-methyl-1-cyclohexanol. This work attracted our attention in connection with the study [2] which we were carrying out under the same conditions for the reduction of D-limonene monoxide (1,2-oxido-8(9)-p-menthene). Here, besides the expected tertiary alcohol, β-terpineol, we also obtained the secondary alcohol D-neohydrocarveol with a high degree of asymmetric purity. Both alcohols were formed in almost equal amounts.

Such a course for the reaction was somewhat unexpected when we considered the analogy between 1-methyl-1-cyclohexene oxide and limonene monoxide; this led us to a serious consideration of the data of Mousseron and co-workers. We decided to repeat carefully the reduction of 1-methyl-1-cyclohexene oxide with special attention to the purity of the starting products. To characterize all of the products which we studied we used combination light-scattering spectra.

1-Methyl-1-cyclohexene needed for preparation of the oxide was prepared by dehydration of 1-methyl-1-cyclohexanol with p-toluene sulfonyl chloride in pyridine solution.*. This dehydration process was very successful. The yield of hydrocarbon in this process was 68%. The combination scattering spectrum of this hydrocarbon had a line $\Delta\nu$ 1673 cm^{-1} corresponding to a secondary-tertiary double bond, and no line at $\Delta\nu$ 1655 cm^{-1} [3] which would show the presence in the mixture of the other possible reaction product, methylene cyclohexane. This indicates the assured homogeneity of the 1-methyl-1-cyclohexene which we synthesized. 1-Methyl-1-cyclohexene oxide, prepared by oxidation of this hydrocarbon with peracetic acid, showed properties identical with those of the oxide which was at the disposal of Mousseron and his co-workers.

The results of the reduction of 1-methyl-1-cyclohexene oxide by lithium aluminum hydride fully confirmed their work [1]: the only reduction product was the tertiary alcohol, 1-methyl-1-cyclohexanol. The combination scattering spectrum of this alcohol contained line $\Delta\nu$ 718 cm^{-1}, characteristic of the pulsating oscillation of the six-membered ring in tertiary alcohols (as distinct from the secondary alcohols in which this oscillation is characterized by a greater value for $\Delta\nu$ [4]).

EXPERIMENTAL

Dehydration of 1-methyl-1-cyclohexanol. The original 1-methyl-1-cyclohexanol was obtained from cyclohexanone and methyl magnesium iodide and was characterized by b.p. 76° at 50 mm, m.p. 24-25°, n_D^{20} 1.4611. A mixture of 43.8 g of 1-methyl-1-cyclohexanol, 36 ml of pyridine, and 48.4 g of p-toluene sulfonyl chloride was heated under reflux for 4 hours at an oil bath temperature of 125-130°. After the reaction mixture had cooled it was treated with water and the reaction product was removed with ether. The ether solution was washed with water and dried with potash. The ether was distilled off and the residue fractionated to give 29.7 g (68%) of 1-methyl-1-cyclohexane, b.p. 110-112° at 756 mm and n_D^{20} 1.4503.

Oxidation of 1-methyl-1-cyclohexene. To a solution of 24 g of 1-methyl-1-cyclohexene in 150 ml of ether was gradually added 250 ml of an ether solution of peracetic acid (containing 40 g of CH_3COOOH). At

*Dehydration with p-toluene sulfonyl chloride was used successfully by one of us in 1950 with L. Vinogradova for preparing myrcene from linalool.

the end, the reaction mixture was neutralized with sodium bicarbonate, the ether solution of the resulting oxide was carefully washed with water and dried over potash. After removal of the ether and fractionation we obtained 14.3 g of 1-methyl-1-cyclohexene oxide with b.p. 69-71° at 82 mm, d_4^{20} 0.9327, n_D^{20} 1.4440.

Reduction of 1-methyl-1-cyclohexene oxide. A solution of 10 g of the oxide in 125 ml of ether was gradually added in a dry nitrogen atmosphere to 100 ml of an ether solution of lithium aluminum hydride (containing 4.56 g of $LiAlH_4$). After 10 min from the end of the addition of the oxide solution the reaction mixture was cooled with ice and 100 ml of water was gradually added to it. The reaction product was extracted with ether from the liquid part of the mixture. The precipitate was treated with a 25% solution of sodium hydroxide and the resulting solution was also extracted with ether. The combined ether extracts were washed with water and dried with potash. After distillation of the ether and fractionation of the residue we obtained 8.7 g (85%) of the substance with b.p. 64-65° at 23 mm, m.p. 24-25°, and n_D^{20} 1.4611, identical with the starting 1-methyl-1-cyclohexanol.

Combined Light Scattering Spectra

Spectrum of 1-methyl-1-cyclohexanol, synthesized from cyclohexanone. $\Delta\nu$: 196 (1), 317 (1), 350 (1), 433 (1), 444 (1), 559 (1), 574 (2), 718 (10), 832 (3), 850 (1), 908 (3), 921 (1), 973 (4), 989 (1), 1011 (2), 1039 (3), 1075 (5), 1090 (5), 1120-1178 (8), 1260 (5), 1276 (5), 1344 (2), 1426-1464 (10), 2864 (4), 2928 (7).

Spectrum of 1-methyl-1-cyclohexanol obtained by reduction of 1-methyl-1-cyclohexene oxide. $\Delta\nu$: 169 (1), 319 (1), 355 (1), 398 (1), 431 (1), 454 (2), 574 (3), 687 (?), 718 (10), 832 (5), 849 (2), 911 (3), 928 (1), 973 (4), 1013 (3), 1040 (2), 1074 (5), 1092(5), 1142-1179 (8), 1260 (5), 1275 (5), 1344 (4), 1387 (1), 1430-1461 (10), 2865 (4), 2930 (7).

Spectrum of 1-methyl-1-cyclohexene. $\Delta\nu$: 209 (1), 297 (?), 333 (1), 423 (3), 437 (3), 493 (2), 533 (1), 565 (1), 619 (4), 673 (1), 759 (10), 793 (2), 818 (3), 858 (4), 890 (2), 963 (2), 998 (3), 1022 (1), 1032 (1), 1051 (2), 1069 (3), 1087 (5), 1136 (6), 1153 (6), 1172 (7), 1237 (1), 1267 (5), 1304 (4), 1334 (1), 1349 (4), 1363 (5), 1422-1456 (10), 1673 (10), 2836 (3), 2909 (6), 2934 (6). (Compare with the data of [5]).

Spectrum of 1-methyl-1-cyclohexene oxide. $\Delta\nu$: 378 (1), 408 (1), 474 (1), 492 (1), 533 (1), 558 (3), 670 (10), 759 (8), 812 (1), 822 (1), 885 (1), 910 (2), 969 (2), 997 (1), 1035 (3), 1058 (1), 1080 (1), 1091 (1), 1182 (5), 1218 (2), 1275 (2), 1306 (2), 1348 (2), 1420-1461 (6), 2657 (2), 2910 (4), 2940 (4). (compare with the data of [6]).

SUMMARY

1. Dehydration of 1-methyl-1-cyclohexanol with p-toluene sulfonyl chloride is a suitable preparative method for obtaining exclusively 1-methyl-1-cyclohexene.

2. The sole product of the reduction of 1-methyl-1-cyclohexene oxide by lithium aluminum hydride is the tertiary alcohol, 1-methyl-1-cyclohexanol. Our data confirm the results obtained by Mousseron and co-workers.

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THE FORMATION OF 5-BENZYLHYDANTOIN-3-ACETYLVALINE FROM THE METHYL ESTER OF N-CARBOBENZOXYPHENYLALANYL-GLYCYLVALINE

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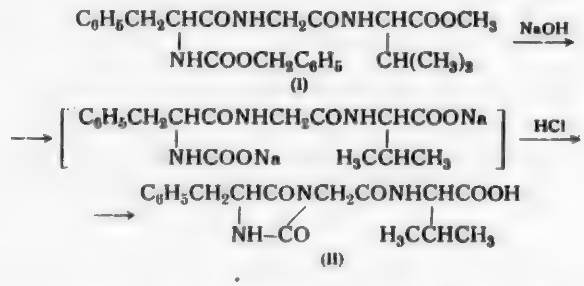
In order to obtain the tripeptide phenylalanylglycylvaline (which was necessary for our further investigations) we prepared the methyl ester of N-carbobenzoxyphenylalanylglycylvaline which was saponified with 1 N sodium hydroxide at 37° under the conditions for saponifying tripeptides [1]. After the solution was acidified with hydrochloric acid and evaporated in a vacuum, besides the expected carbobenzoxyphenylalanylglycylvaline, a white, crystalline substance, melting at 237-240° was isolated. It gave an intense carbonyl reaction with picric acid; the ninhydrin and biuret reactions were negative. After complete hydrolysis with 25% sulfuric acid the substance gave a hydrolyzate which was separated by paper chromatography into phenylalanine, glycine and valine. Reduction of the substance with hydrogen in the presence of Pd black under the conditions for the removal of the carbobenzoxy group did not change it. Analysis and further study of the properties of this substance led to the conclusion that when the methyl ester of carbobenzoxyphenylalanylglycylvaline (I) was saponified by 1 N sodium hydroxide and then acidified and evaporated in a vacuum it formed 5-benzylhydantoin-3-acetylvaline (II). Thus, when the methyl ester of N-carbobenzoxyphenylalanylglycylvaline is saponified, there is simultaneous splitting off of methyl and benzyl alcohols. The unstable carbamic acid of the tripeptide thus formed is transformed into the hydantoin.

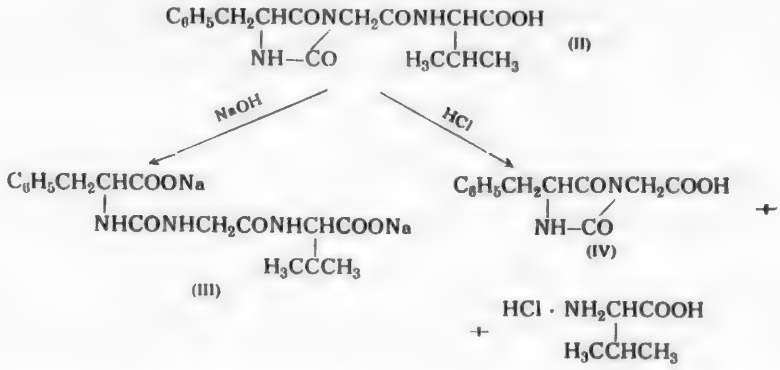


(1)

5-Benzylhydantoin-3-acetylvaline dissolves in 0.1 N NaOH with weak heating to combine with 2 moles of alkali. It may be that there occurs opening of the hydantoin ring with formation of the sodium salt of carbonyl bis-phenylalanine-(glycylvaline) (III). When 5-benzylhydantoin-3-acetylvaline is heated with hydrochloric acid (1 : 1), the ring is not broken, but valine is split off and 5-benzylhydantoin-3-acetic acid (IV) is formed.

The formation of hydantoincarboxylic acids from esters of carboalkoxydipeptides has been described in the literature. Thus, Fruton and Bergmann [2] treated the ethyl ester of carbobenzoxy-L-phenylalanylglycine in alcohol solution with ammonia and obtained the amide of 5-benzylhydantoin-3-acetic acid, from which 5-benzylhydantoin-3-acetic acid was isolated by boiling with sulfuric acid. In an analogous way the esters of carbobenzoxyleucylglycine gave the amide of 5-isobutylhydantoin-3-acetic acid [3]. Wessely and co-workers [4] saponified the ester of carbomethyoxyphenylalanylphenylalanine with 1 N sodium hydroxide on the heated water bath and by later acidification of the solution obtained carbonyl bisphenylalanine. Saponification of

the esters of carbomethoxyalanylglycine and carbomethoxyglycylalanine under the same conditions gave the identical compound, carbonyl bisglycine (alanine). The authors assumed the formation of hydantoin as an intermediate compound. Earlier, Granacher and Landolt [5] showed the possibility of transforming diamides and esters of carbonyl bisglycine into hydantoin-3-acetic acid by heating on the water bath with hydrochloric acid, and the resulting hydantoin was not destroyed by boiling with hydrochloric acid (1 : 1).



(2)

The formation of 5-benzylhydantoin-3-acetylvaline from the methyl ester of carbobenzoxyphenylalanylglycylvaline thus is in accord with the literature data. However, it is interesting to observe that in the saponification of the methyl ester of carbobenzoxyphenylalanylvalylglycine, which differs in the order of the amino acids, using 1 N sodium hydroxide under the conditions described above, we obtain carbobenzoxyphenylalanylvalylglycine in good yield; the formation of a hydantoin is not found.

EXPERIMENTAL

Obtaining the methyl ester of N-carbobenzoxyphenylalanylglycylvaline [6]. To 14 g of cbz-phenylalanine * and 7.7 ml of triethylamine in 100 ml anhydrous chloroform cooled to 0° was added 3.5 ml of ethyl chlorocarbonate. After 10 min the reaction mixture was treated in portions with stirring with a cold solution of 10.6 g of methyl glycylvalinate hydrochloride and 6.5 ml of triethylamine in 75 ml of chloroform. The mixture stood 1 hour at 0° and then another hour at 20°. The chloroform solution was washed with 1 N HCl, water, 3% $NaHCO_3$ solution, and again with water, dried over Na_2SO_4, and evaporated in a vacuum. A light yellow oil crystallized after treatment with ether. The white crystals, melting at 104°, were easily soluble in methyl and ethyl alcohol. The yield of methyl ester of N-cbz-phenylalanylglycylvaline was 19.1 g (87%).

Found %: N 9.06, 8.88. $C_{25}H_{31}O_6N_3$. Calculated %: N 8.95.

The absorption maximum for the copper complex of the methyl ester of N-cbz-phenylalanylglycylvaline lay in the interval 530-540 mμ.

Saponification of the methyl ester of N-cbz-phenylalanylglycylvaline and formation of 5-benzylhydantoin-3-acetylvaline. 7 g of the methyl ester of N-cbz-phenylalanylglycylvaline was dissolved in 100 ml of methanol. The solution was placed in a thermostat at 37° and treated with 54 ml of 1 N NaOH (at first 30 ml, after 2 hours, 12 ml, then after 1 hour, 6 ml, and at the end of the 4th hour, 6 more ml of 1 N NaOH). Then the solution was diluted with 100 ml of water and acidified to Congo with 5 N HCl. An emulsion formed and was treated with ether. The acid aqueous solution was evaporated in a vacuum to small volume. The white precipitate was filtered, washed with water, and dried. We obtained 4.85 g of substance which after recrystallization from hot water melted at 237-240°. It gave an intense carbonyl reaction with picric acid in soda solution; the ninhydrin and biuret reactions were negative. The yield of 5-benzylhydantoin-3-acetylvaline was 93%.

Found %: C 58.75, 58.93; H 6.16, 6.26; N 12.36, 12.15. $C_{17}H_{21}O_5N_3$. Calculated %: C 58.75; H 6.05; N 12.11.

*Carbobenzoxy is shortened to cbz.

Hydrolysis of 5-benzylhydantoin-3-acetylvaline. A small amount of 5-benzylhydantoin-3-acetylvaline was hydrolyzed by heating with 25% H_2SO_4 in a sealed tube for 10 hours at 135-140°. The neutralized hydrolyzate was submitted to paper chromatography; in an n-butanol-water-acetic acid (4 : 5 : 1) solvent. After the chromatogram was developed with a solution of ninhydrin in n-butyl alcohol it showed three spots, corresponding to phenylalanine, glycine and valine.

Hydrogenation of 5-benzylhydantoin-3-acetylvaline. A small amount of 5-benzylhydantoin-3-acetylvaline was reduced by hydrogen in the presence of Pd black in methanol with addition of glacial acetic acid. After evaporation of the filtrate in a vacuum we obtained a white powder which gave an intense carbonyl reaction with picric acid. The ninhydrin and biuret reactions were negative. M.p. 237°. A mixed melting point with the starting 5-benzylhydantoin-3-acetylvaline showed no depression.

Action of 0.1 N NaOH on 5-benzylhydantoin-3-acetylvaline. 0.0762 g 5-benzylhydantoin-3-acetylvaline was dissolved with slight heating on a water bath in 7.71 ml of 0.1 N NaOH. The excess alkali was titrated with 3.3 ml of 0.1 N H_2SO_4. The reaction used 4.41 ml of 0.1 N NaOH; 1 mole of 5-benzylhydantoin-3- acetylvaline combined with 2 moles of NaOH.

Action of HCl on 5-benzylhydantoin-3-acetylvaline. 0.15 g of 5-benzylhydantoin-3-acetylvaline was boiled for 3 hours with 10 ml of HCl (1 : 1). The solution was extracted with ether until the carbonyl reaction vanished in the water solution. The ether extract was dried over Na_2SO_4 and evaporated dry in a vacuum. We obtained 0.07 g of white crystalline substance. After recrystallization from hot water it melted at 181-182°. The melting point of 5-benzylhydantoin-3-acetic acid is 181° [5].

A small amount of the substance was hydrolyzed with 25% H_2SO_4 for 10 hours at 130-140°. The hydrolyzate was studied by paper partition chromatography; solvent n-butanol–water–acetic acid (4 : 5 : 1). Spots for phenylalanine and glycine were found on the chromatogram.

The acid water solution was evaporated dry in a vacuum. The residue was valine hydrochloride, a white crystalline substance, m.p. 187-189°; according to the literature it melts at 189°. The yield was 0.05 g (100%). Paper chromatography with the same solvent gave only one spot, corresponding to valine.

SUMMARY

We have described the formation of 5-benzylhydantoin-3-acetylvaline from the methyl ester of N-carbobenzoxyphenylalanylglycylvaline.

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THE SYNTHESIS OF CYANOMETHYL ESTERS OF PEPTIDES AND THEIR USE IN OBTAINING PEPTIDES

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Recently Schwyzer and co-workers have presented a new method for the synthesis of peptides. They studied a whole series of activated esters of hippuric acid in the reaction with benzylamine and found the most reactive acylating agents to be the cyanomethyl esters [1]. In later communications [2-5] these authors studied the possibility of using the cyanomethyl esters in the synthesis of peptides in more complex models. They showed that the cyanomethyl esters of amino acid and peptide derivatives were easily obtained, could be isolated in crystalline form, were sufficiently active and stable, and offered the possibility of carrying out the synthesis of peptides at room temperature. The use of the cyanomethyl esters of peptides for obtaining cyclopeptides was especially interesting [6].

In the present work we have obtained the cyanomethyl esters of some carbobenzoxy derivatives of amino acids, dipeptides, and tripeptides, and studied their usefulness in the synthesis of peptides and their stability when the carbobenzoxy group was removed by hydrogen bromide in glacial acetic acid.

The cyanomethyl esters were obtained by reaction of cbz-amino acids * or cbz-peptides with chloroacetonitrile in the presence of triethylamine with heating to 60-70°. The canomethyl esters were prepared from: cbz-phenylalanine, cbz-phenylalanylglycine, cbz-phenylalanylglycylleucine, cbz-glycylphenylalanine, cbz-glycylphenylalanylleucine, cbz-glycylleucylphenylalanine. The results of the experiments are given in Table 1.

TABLE 1

Cyanomethyl ester of the compounds	Formula	Yield %	Melting point
cbz-Phenylalanine	$C_{19}H_{18}O_4N_2$	80.9	98—99°
cbz-Phenylalanylglycine	$C_{21}H_{21}O_5N_3$	72.0	100—101
cbz-Glycylphenylalanine	$C_{21}H_{21}O_5N_3$	84.7	70—72
cbz-Phenylalanylglycylleucine	$C_{27}H_{32}O_6N_4$	65.2	113—114
cbz-Glycylphenylalanylleucine	$C_{27}H_{32}O_6N_4$	78.1	110—111
cbz-Glycylleucylphenylalanine	$C_{27}H_{32}O_6N_4$	74.8	127—129

As these data show, the cyanomethyl esters of the carbobenzoxy derivatives of peptides are obtained in good yield and in the crystalline state.

The synthesis of peptides by the use of the cyanomethyl esters of carbobenzoxy amino acids or peptides proceeds in anhydrous chloroform in the reaction with the methyl esters of amino acid or peptide hydrochlorides

* Carbobenzoxy is shortened to cbz.

in the presence of triethylamine and small amounts of glacial acetic acid. Below we give comparative data on the synthesis of peptides using cyanomethyl esters and using the method of Boissonnas through mixed anhydrides of cbz-amino acids and ethyl carbonate combined with the methyl esters of the hydrochlorides of amino acids or peptides in the presence of triethylamine (Table 2).

TABLE 2

Reacting compounds		Peptides obtained		
I	II	Name	Yield, %	Melting point
Cyanomethyl ester of cbz-phenylalanine	Methyl glycinate hydrochloride	Methyl ester of cbz-phenylalanylglycine	79.0	114–115°
cbz-Phenylalanine	The same	The same	78.3	114–115
Cyanomethyl ester of cbz-phenylalanine	Methyl glycylleucinate hydrochloride	Methyl ester of cbz-phenylalanylglycylleucine	50.0	114–118
cbz-Phenylalanylglycine	Methyl leucinate hydrochloride	The same	76.2	117–118
Cyanomethyl ester of cbz-glycine	Methyl phenylalaninate hydrochloride	Methyl ester of cbz-glycylphenylalanine	85.0	80–82
cbz-Glycine	Methyl leucinate hydrochloride	Methyl ester of cbz-glycylleucine	88.6	–
cbz-Glycylphenylalanine	The same	Methyl ester of cbz-glycylphenylalanylleucine	63.9	93–95
cbz-Glycylleucine	Methyl phenylalaninate hydrochloride	Methyl ester of cbz-glycylleucylphenylalanine	55.3	118–120

The results show that the method of cyanomethyl esters can be used for the synthesis of peptides just as can the widely used method of Boissonnas.

In the present work we present experiments on the removal of the carbobenzoxy group in the cyanomethyl esters of cbz-tripeptides by the action of hydrogen bromide in glacial acetic acid (Table 3).

TABLE 3

Cyanomethyl ester of tripeptide hydrobromide	Formula	% yield	Melting point
Cyanomethyl ester of phenylalanylglycylleucine hydrobromide	$C_{19}H_{27}O_4N_4Br$	89.4	192–193° (decomp)
Cyanomethyl ester of glycylphenylalanylleucine hydrobromide	$C_{19}H_{27}O_4N_4Br \cdot 6H_2O$	86.4	–
Cyanomethyl ester of glycylleucylphenylalanine hydrobromide	$C_{19}H_{27}O_4N_4Br$	61.5	197–198° (decomp)

The resulting cyanomethyl esters of tripeptide hydrobromides were hygroscopic and contained water of crystallization. In the case of the cyanomethyl ester of glycylphenylalanylleucine hydrobromide the water could not be removed after prolonged drying over P_2O_5 in a vacuum at 60°.

EXPERIMENTAL

Cyanomethyl ester of cbz-phenylalanine. 7.5 g of cbz-phenylalanine was mixed with 5.25 ml of triethylamine and 4.75 ml of chloroacetonitrile. The resulting viscous mass was heated for one half hour to 70° on a water bath and then allowed to stand overnight at 20°. Then the reaction mixture was treated with ethyl acetate. The resulting precipitate of trimethylamine hydrochloride was filtered off and the ethyl acetate solution was washed with dilute HCl, a 3% solution of $NaHCO_3$, and water, dried over ignited Na_2SO_4, and evaporated in a vacuum. The remaining oil crystallized when absolute ether was added. We obtained 6.8 g of the cyanomethyl ester of cbz-phenylalanine. After reprecipitation from aqueous methanol it melted at 98-99°.

Found %: N 8.34, 8.27. $C_{19}H_{18}O_4N_2$. Calculated %: N 8.28.

Methyl ester of cbz-phenylalanylglycine. A) A solution of 15 g of the cyanomethyl ester of cbz-phenylalanine in 100 ml of anhydrous chloroform was treated with 8.3 g of methyl glycinate hydrochloride, 18.3 ml of triethylamine, and 0.29 ml of glacial acetic acid. After standing for 64 hours at 20°, the solution was washed with dilute HCl, water, 3% $NaHCO_3$, water, dried over Na_2SO_4, and evaporated in a vacuum. The remaining oil crystallized when it stood with ether. We obtained 12.4 g of the methyl ester of cbz-phenylalanylglycine.

B) The methyl ester of cbz-phenylalanylglycine was obtained by the method of Boissonnas: a solution of 7.5 g of cbz-phenylalanine and 3.9 g triethylamine in 75 ml of anhydrous chloroform was cooled to −5° and 2.7 ml of ethyl chlorocarbonate awas added. After 10 min the reaction mixture was treated with a cooled solution of 3.55 g of methyl glycinate hydrochloride and 3.9 ml of triethylamine in 100 ml of anhydrous chloroform in portions with stirring. The reaction mixture stood for 1 hour in an ice bath and then was kept for 2 hours at 20°. After washing the solution with dilute HCl, water, 3% $NaHCO_3$, and again water, it was dried over Na_2SO_4 and evaporated in a vacuum to give 7.25 g of the methyl ester of cbz-phenylalanylglycine. After drying over P_2O_5 at 10 mm the compound melted at 114-115°.

Found %: N 7.61. $C_{20}H_{22}O_5N_2$. Calculated %: N 7.56.

cbz-Phenylalanylglycine. A suspension of 4.6 g of the methyl ester of cbz-phenylalanylglycine in 50 ml of methanol and 7.4 ml of 2 N NaOH was shaken for 1 hour at 20°. The solution was diluted with water and acidified with 5 N HCl to Congo. We obtained 4 g (90.9%) of cbz-phenylalanylglycine, m.p. 154-155°.

Found : equiv. 351.3. $C_{19}H_{20}O_5N_2$. Calculated; equiv. 356.

Cyanomethyl ester of cbz-phenylalanylglycine. A mixture of 1.38 g of cbz-phenylalanylglycine, 0.79 g of triethylamine, and 0.71 ml of chloroacetonitrile was kept at 60° and treated in the usual way (cf. cyanomethyl ester of cbz-phenylalanine). We obtained 1.08 g of the cyanomethyl ester of cbz-phenylalanylglycine.

Found %: N 10.55, 10.47. $C_{21}H_{21}O_5N_3$. Calculatdd %: N 10.63.

Methyl ester of cbz-phenylalanylglycylleucine. A) To a solution of 3.15 g of the canomethyl ester of cbz-phenylalanine in 50 ml of anhydrous chloroform was added 3.5 g of the methyl ester of glycylleucine hydrochloride, 3.9 ml of triethylamine, and 0.06 ml of glacial acetic acid. The reaction mixture stood at 20° for 72 hours. The solution was treated in the usual way. After removal of the solvent in a vacuum, an oil remained and crystallized when it stood with anhydrous ether. We obtained 2.25 g of the methyl ester cf cbz-phenylalanylglycylleucine.

B) Using the Boissonnas method we combined 9.77 g cbz-phenylalanylglycine and 5.7 g of methyl leucinate hydrochloride in 170 ml of anhydrous chloroform in the presence of 8.7 ml of triethylamine and 3 ml of ethyl chlorocarbonate to obtain 10.06 g of the methyl ester of cbz-phenylalanylglycylleucine.

Found %: N 8.73, 8.40. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.68.

cbz-Phenylalanylglycylleucine. A suspension of 5.9 g of the methyl ester of cbz-phenylalanylglycylleucine in 7.3 ml of 2 N NaOH and 50 ml of methanol was kept for 10 hours at 20°. At the edd of the 10th hour the solution was increased by 1.5 ml more of 2 N NaOH, and then the solution was diluted with water and acidified with 5 N HCl. The oil which precipitated was extracted with ether, the ether solution was dried over Na_2SO_4 and evaporated in a vacuum. An oil remained which was dissolved in a minimum amount of

methanol and was precipitated by water. We obtained 4.48 g (78.3%) of cbz-phenylalanylglycylleucine, m.p. 74-75°.

Found %: C 63.68, 63.54; H 6.97, 6.81. $C_{25}H_{31}O_6N_3$. Calculated %: C 63.96; H 6.61.

Cyanomethyl ester of cbz-phenylalanylglycylleucine. A mixture of 3 g of cbz-phenylalanylglycylleucine, 1.3 ml of triethylamine and 1.2 ml of chloroacetonitrile was heated for 4 hours on the water bath at 70° and then stood overnight at 20°. After the usual treatment we obtained an oil which crystallized in ether. The yield of cyanomethyl ester of cbz-phenylalanylglycylleucine was 2.12 g.

Found %: N 11.07, 10.75. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of pnehylalanylglycylleucine hydrobromide. To 2 g of the cyanomethyl ester of cbz-phenylanylglycylleucine was added 2.8 ml of glacial acetic acid saturated with HBr. After an hour (at the end of evolution of bubbles of CO_2) the reaction mixture had the appearance of a yellow oil and 100 ml of anhydrous ether was added to it. When the oil was stirred with the ether, it crystallized. After three reprecipitations by ether from anhydrous methanol, 1.52 g of the cyanomethyl ester of phenylalanylglycylleucine hydrobromide was obtained. The compound gave a positive hydroxamic reaction; its nature was confirmed by paper chromatography. The hydrobromide was hygroscopic, although it did not deliquesce in air.

Found %: N 11.83, 11.73. $C_{19}H_{27}O_4N_4Br \cdot H_2O$. Calculated %: N 11.83.

The substance was dried for a week over P_2O_5 at 10 mm and 60°.

Found %: N 12.2, 12.39. $C_{19}H_{27}O_4N_4Br$. Calculated %: N 12.3.

Methyl ester of cbz-glycylphenylalanine. 5 g of cyanomethyl ester of cbz-glycine [2] was dissolved in 40 ml of anhyrous chloroform. To the solution was added 5.2 g of methyl phenylalaninate hydrochloride, 4.30 ml of triethylamine, and 0.13 ml of glacial acetic acid. The reaction mixture stood at 20° for 50 hours. After the usual treatment we obtained an oil which crystallized when it stood with anhydrous ether. The methyl ester of cbz-glycylphenylalanine was obtained in the form of white silky needles.

Found %: N 7.73, 7.40. $C_{20}H_{22}O_5N_2$. Calculated %: N 7.56.

cbz-Glycylphenylalanine. To a suspension of 3.7 g of the methyl ester of cbz-glycylphenylalanine in 40 ml of methanol was added 6 ml of 2 N NaOH. The reaction mixture stood for an hour at 20°. The clear solution was diluted with water and acidified with 0.72 ml of glacial acetic acid. The white, crystalline precipitate was filtered, washed with water, and dried in a vacuum desiccator over H_2SO_4. We obtained 3 g (84.2%) of cbz-glycylphenylalanine, m.p. 155-156°.

Found: equiv. 356. $C_{19}H_{20}O_5N_2$. Calculated: equiv. 356.

Cyanomethyl ester of cbz-glycylphenylalanine. A mixture of 1.1 g of cbz-glycylphenylalanine, 0.56 ml of chloroacetonitrile, and 0.62 ml of triethylamine was heated at 60° for 2 hours and then stood overnight at 20°. After the usual treatment we obtained 1 g of cyanomethyl ester of cbz-glycylphenylalanine.

Found %: N 10.76, 10.83. $C_{21}H_{21}O_5N_3$. Calculated %: CN 10.63.

Methyl ester of cbz-glycylphenylalanylleucine. 5.6 g of cbz-glycylphenylalanine was combined by the Boissonnas method with 3.3 g of methyl leucinate hydrochloride in 150 ml of anhydrous chloroform in the presence of 5 ml of triethylamine and 1.7 ml of ethyl chlorocarbonate with cooling. After the usual treatment we obtained 4.85 g of the methyl ester of cbz-glycylphenylalanylleucine.

Found %: N 8.90, 8.90. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.69.

cbz-Glycylphenylalanylleucine. A mixture of 4.3 g of methyl ester of cbz-glycylphenylalanylleucine and 5.3 ml of 2 N NaOH in 35 ml of methanol was kept for 5 hours at 20°. The clear solution was treated with water and acidified with 5 N HCl to Congo. We obtained 3.52 g (85.8%) of cbz-glycylphenylalanylleucine, m.p. 140-141°.

Found: equiv. 470. $C_{25}H_{31}O_6N_3$. Calculated: equiv. 469.

Cyanomethyl ester of cbz-glycylphenylalanylleucine. A mixture of 3.37 g of cbz-glycylphenylalanylleucine, 1.46 ml of triethylamine, and 1.33 ml of chloroacetonitrile stood 36 hours at 20° and then was heated

3 hours at 60 – 70° and treated in the usual way. We obtained an oil which crystallized in ether. The yield of cyanomethyl ester of cbz-glycylphenylalanylleucine was 2.82 g. After reprecipitation from aqueous methanol and drying in a vacuum desiccator over H_2SO_4, it melted at 110-111°.

Found %: N 11.01. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of glycylphenylalanylleucine hydrobromide. 2.4 g of cyanomethyl ester of cbz-glycylphenylalanylleucine was treated with 3.4 ml of glacial acetic acid saturated with HBr. After 2.5 hours (at the end of evolution of CO_2) the reaction mixture was treated with 100 ml of anhydrous ether and the mixture stood overnight in the cold (–10°). The oil which precipitated was washed free of excess HBr by repeated reprecipitations from methanol with anhydrous ether. Then the oil was dissolved in 10 ml of water, the solution was extracted with ether, and evaporated to dryness in a vacuum. The colorless oil which remained was treated several times with ethyl alcohol and acetone. After removal of the solvents in a vacuum there remained a white, amorphous substance which quickly deliquesced in air. The homogeneity of the cyanomethyl ester of glycylphenylalanylleucine hydrobromide which we obtained was shown by paper chromatography. The hydroxamic reaction was positive. Yield 1.85 g.

Found %: N 9.56, 9.62. After repeated drying over P_2O_5 at 10 mm and 60° and analytical data were almost unchanged.

Found %: N 9.79, 9.70. $C_{19}H_{27}O_4N_4Br \cdot 6H_2O$. Calculated %: N 9.94.

Methyl ester of cbz-glycylleucine. 10.45 g cbz-glycine was combined by the Boissonnas method with 9.1 g methyl leucinate hydrochloride in 150 ml of chloroform in the presence of 15.2 ml of triethylamine and 5.7 ml of ethyl chlorocarbonate with cooling. The reaction mixture was kept for 1 hour in an ice bath, then for 2 hours at 20° and then was treated in the usual way. We obtained a colorless oil. The yield of methyl ester of cbz-glycylleucine was 14.87 g.

Found %: N 8.21, 8.07. $C_{17}H_{24}O_5N_2$. Calculated %: C 8.33.

cbz-Glycylleucine. 10.08 g methyl ester of cbz-glycylleucine was dissolved in 150 ml of anhydrous methanol and to the solution was added 44 ml of 1 N NaOH. After 30 min the clear solution was acidified with 5 N HCl to Congo, and diluted with water to full precipitation of cbz-glycylleucine. We obtained 7.1 g (73.5%) of substance melting at 123-124°.

Found: equiv. 323, 315. $C_{16}H_{22}O_5N_2$. Calculated: equiv. 322.

Methyl ester of cbz-glycylleucylphenylalanine. 9.45 g of cbz-glycylleucine and 6.15 g of methyl phenylalaninate hydrochloride were combined by the Boissonnas method in the presence of 8.8 ml of triethylamine and 125 ml of anhydrous chloroform with 3.23 ml of ethyl chlorocarbonate with cooling. After the usual treatment we obtained 7.75 g of methyl ester of cbz-glycylleucylphenylalanine. After reprecipitation from methanol by water it melted at 118-120°.

Found %: N 8.79, 8.54. $C_{26}H_{33}O_6N_3$. Calculated %: N 8.69.

cbz-Glycylleucylphenylalanine. 7.75 g of the methyl ester of cbz-glycylleucylphenylalanine was shaken for 1 hour with 9.6 ml of 2 N NaOH in 65 ml of methanol at 20°. The solution stood another hour at 20° and then was diluted with water and acidified with 5 N HCl. We obtained 7 g (93.3%) cbz-glycylleucylphenylalanine with m.p. 152-154°.

Found: equiv. 472. $C_{25}H_{31}O_6N_3$. Calculated: equiv. 469.

Cyanomethyl ester of cbz-glycylleucylphenylalanine. A mixture of 1.2 of cbz-glycylleucylphenylalanine, 0.52 ml of triethylamine, and 0.47 ml of chloroacetonitrile was kept for 12 hours at 20°, then was heated for 2 hours at 70°. After the usual treatment we obtained 0.95 g of cyanomethyl ester of cbz-glycylleucylphenylalanine with m.p. 107-122°. After reprecipitation from methanol by water the compound melted at 127-129°.

Found %: N 11.09, 10.91. $C_{27}H_{32}O_6N_4$. Calculated %: N 11.02.

Cyanomethyl ester of glycylleucylphenylalanine hydrobromide. 2.1 g of cyanomethyl ester of cbz-glycylleucylphenylalanine was treated with 2.1 ml of acetic acid saturated with HBr, and kept 30 min at 20°.

Then to the mixture was added 10 ml of anhydrous methanol and after 20 min, 100 ml of anhydrous ether. A yellow oil precipitated. After twice reprecipitating from alcohol by ether we obtained 1.15 g of cyanomethyl ester of glycylleucylphenylalanine hydrobromide. The homogeneity of the compound was shown by paper chromatography. The hydroxamic reaction was positive.

Found %: N 11.30, 11.19. $C_{19}H_{27}O_4N_4Br \cdot 2H_2O$. Calculated %: N 11.40.

The substance was dried over P_2O_5 at 10 mm and 60°.

Found %: N 12.35. $C_{19}H_{27}O_5Br$. Calculated %: N 12.30.

SUMMARY

We have described the synthesis of cyanomethyl esters of carbobenzoxy derivatives of peptides and their use in preparing peptides. We have synthesized cyanomethyl esters of: carbobenzoxyphenylalanine, carbobenzoxyphenylalanylglycine, carbobenzoxyglycylphenylalanine, carbobenzoxyphenylalanylglycylleucine, carbobenzoxyglycylphenylalanylleucine, and carbobenzoxyglycylleucylphenylalanine.

We have obtained the peptide derivatives: methyl ester of carbobenzoxyphenylalanylglycine, methyl ester of carbobenzoxyglycylphenylalanine, methyl ester of carbobenzoxyglycylleucine, and methyl ester of carbobenzoxyphenylalanylglycylleucine.

We have isolated the hydrobromides of the cyanomethyl esters of the tripeptides: phenylalanylglycylleucine, glycylphenylalanylleucine, and glycylleucylphenylalanine.

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STUDIES IN THE FIELD OF THE CHEMISTRY OF THE CYANINE DYES

XIII.* THIACYANINES WHICH CONTAIN UNSATURATED RADICALS AS SUBSTITUENTS IN THE 6,6'-POSITIONS OF BENZTHIAZOLE

I. K. Ushenko and S. E. Gornostaeva

In the present communication we describe the synthesis of thiacarbocyanines which contain, in the 6,6'-positions of the benzthiazole, unsaturated radicals (styryl, p-methoxystyryl, and α-thienylvinyl). It is assumed that the introduction of unsaturated radicals into the benzthiazole nucleus of the dyes will lengthen the chromophore and deepen the color of the thiacarbocyanine. Cyanine dyes of this type have not been known before.

The synthesis of the starting bases was carried out by the Meerwein reaction, by the action of diazotized 2-methyl-6-aminobenzthiazole on unsaturated acids.

In the reaction of aryl diazonium halides with α,β-unsaturated carbonyl compounds, Meerwein [1] obtained α-halo-β-arylalkanes or alkenes. The reaction goes in a water-acetone solution in the presence of catalytic amounts of cupric chloride. The large number of unsaturated compounds which were introduced into this reaction could be assigned to the classes: simple ethylenes [2,7], aromatic ethylenes [3], α,β-unsaturated carbonyl compounds [4], cinnamic acid and its derivatives [1, 5], coumarins [1], acrylic acid [6], acrylonitrile [4, 8, 9], acetylenes [1, 2], dienes with conjugated bonds [10], and benzoylacrylic acid [11].

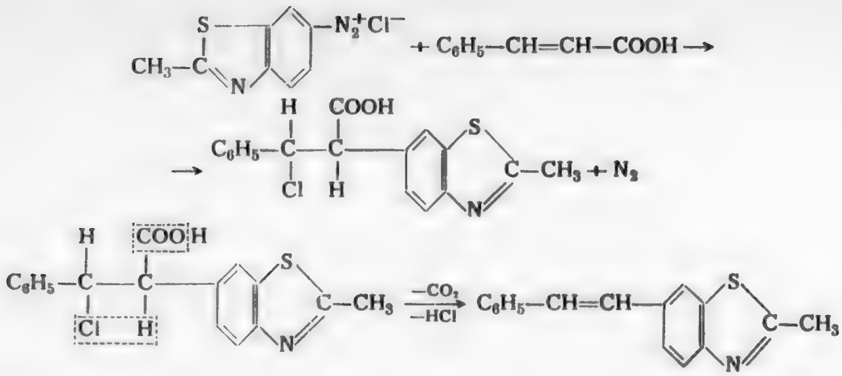
The mechanism of this interesting reaction was the subject of much discussion [8, 9, 12]. The discussion centered around two points: 1) the character of the reaction (homolytic or heterolytic), 2) the role of the divalent copper and the specificity of the acetone in this reaction. Recently Kochi has published some work [13] in which he gives a mechanism and the kinetics of the Meerwein reaction. Kochi showed that the Meerwein reaction could proceed also in a water-alcohol solution, but the yield of arylation products was considerably lower. Attempts to carry out the Meerwein reaction in the absence of copper salts in a water-acetone solution were unsuccessful [8].

Heterocyclic diazo compounds until now have not been introduced into reaction with unsaturated compounds. We were concerned with this type of investigation, and first we took an amine of the benzthiazole series, 2-methyl-6-aminobenzthiazole. In the reaction of diazotized 2-methyl-6-aminobenzthiazole with cinnamic, p-methoxycinnamic, and α-thienylacrylic acids under the conditions of the Meerwein reaction, we succeeded in obtaining three new basic derivatives of 2-methyl-benzthiazole which contained unsaturated substituents in the 6-position.

At the time when we carried out the reaction we observed the evolution of nitrogen and carbon dioxide. Among the reaction products, aside from benzthiazoles with unsaturated radicals, we observed 2-methyl-6-chlorobenzthiazole, chloroacetone, and azo compounds.

The synthesis of 2-methyl-6-styrylbenzthiazole could be presented thus:

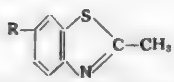
*Communication XII in Ukrain. Khim. Zhur. 22, 76 (1956).

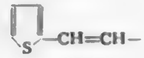


2-Methyl-6-styrylbenzthiazole was also obtained by reaction of styrene with benzthiazolene diazonium chloride. The yield did not exceed 3-4%.

Table 1 gives the new bases which we synthesized.

TABLE 1



R	% Yield of basic product	Melting point of basic product	Yield of byproducts (in g): chloroacetone	Yield of byproducts (in g): 2-methyl-6-chlorobenzthiazole	Amount of unreacted acrylic acid
$C_6H_5-CH=CH-$	17	118°	2	2.3	1.7
	6.8	170—171	—	1.2	7
	9.5	119—120	—	0.3	2.2

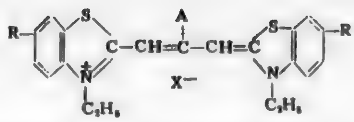
The low yield of benzthiazole which contains unsaturated groups in position 6 can be explained by the fact that a number of side reactions occur.

The amount of unreacted acid depends strongly on its solubility in acetone. The poorer the solubility of the acid in acetone, the less the yield of styryl benzthiazole. In order to reduce the side reactions to a minimum we had to observe a number of conditions, chiefly reaction temperature and acidity of the solution. The activity of the unsaturated compounds used in the reaction was also very important.

When the bases were heated with dimethyl or diethyl sulfate, decomposition products were formed along with the quaternary salts. Therefore the quaternary salts were obtained by heating the bases with methyl or ethyl p-toluenesulfonate. When the quaternary salts were condensed with orthoesters we obtained thiacarbocyanines which are shown in Table 2. For comparison we also give 3,3'-diethylthiacarbocyanine.

Table 2 shows that the introduction of unsaturated substituents in the 6,6'-positions of thiacarbocyanines sharply changes the absorption maxima in the long wave portion of the spectrum (by 37-47 mμ). The introduction of the methoxy group in the position para to the styryl radical causes a further shift in the absorption spectrum of the long wave portion by 10 mμ. Thus the effect of the p-methoxystyryl and the α-thienylvinyl radical on the color is almost the same.

TABLE 2

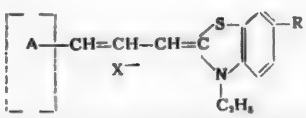


Compound No.	R	A	Absorption maximum (in mμ)
	H	H	558
(I)	$C_6H_5-CH=CH-$	H	595
(II)		CH_3	580
(III)		C_2H_5	585
(IV)		H	605
(V)		C_2H_5	596
(VI)		H	606
(VII)		C_2H_5	598

Quaternary salts were also produced by condensation with the ethyl p-toluenesulfonate of 2-(β-acetanilidovinyl)-4,5-benzobenzthiazole and 2-(β-acetanilidovinyl)-5-methoxybenzthiazole, from which we obtained five unsymmetrical thiacarbocyanines, shown in Table 3.

Besides these we also obtained three rhodacyanines which are shown in Table 4.

TABLE 3



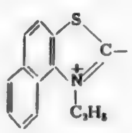
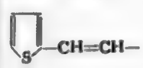
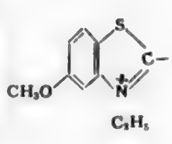
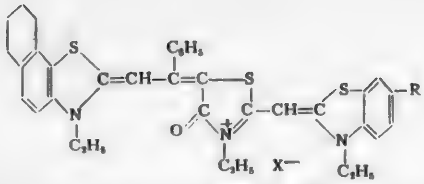
Compound No.	A	R	Absorption maximum (in mμ)
		H	581
(VIII)		$C_6H_5-CH=CH-$	596
(IX)			601
(X)			600
(XI)		$C_6H_5-CH=CH-$	589
(XII)			595

TABLE 4



Compound No.	R	Absorption maximum (in mμ)
	H	612
(XIII)	C_6H_5–CH=CH–	627
(XIV)	CH_3O–C_6H_4–CH=CH–	631
(XV)	2-thienyl–CH=CH–	633

From the results in Tables 3 and 4 it is evident that in unsymmetrical cyanine dyes the introduction of unsaturated groups in position 6 of the benzthiazole ring also causes a considerable shift of the absorption maximum in the long wave portion of the spectrum.

EXPERIMENTAL

α-Thiophene aldehyde was obtained from thiophene, N-ethyl formanilide, and phosphorus oxychloride [14, 15].

2-Thienylacrylic acid was prepared from α-thiophene aldehyde and malonic acid [16].

p-Methoxy cinnamic acid was obtained from anisaldehyde and malonic acid [17].

2-Methyl-6-aminobenzthiazole was obtained by reduction of 2-methyl-6-nitrobenzthiazole.

2-Methyl-6-styrylbenzthiazole from cinnamic acid. 16.4 g of 2-methyl-6-aminobenzthiazole was dissolved in 25 ml of hydrochloric acid (d 1.19) and 20 ml of water. The solution was cooled to −5° and diazotized with 7.5 g of sodium nitrite in 12 ml of water. At the same time a three-necked flask was fitted with a thermometer, stirrer, and stopper, and in it was placed a mixture of 14.8 g of cinnamic acid, 120 ml of acetone, 24 g of crystalline sodium acetate, and 5.1 g of cupric chloride ($CuCl_2 \cdot 2H_2O$) in 10 ml of water. The mixture was cooled to −5°, and to the resulting suspension with stirring was added the prepared solution of diazonium chloride over a period of 30 min. The flask was then connected with a Tishchenko flask with a barium hydroxide solution. The mixture was stirred at −2° for 2 hours, and then for 4-5 hours more during which the temperature gradually rose to that of the room. At −2° slow evolution of a gaseous product began, at 0° this became intense, and after some time a copious precipitate of barium carbonate appeared in the Tishchenko flask. On the next day the mixture was steam distilled, the acetone was collected separately, and the residual distillate (about 2 liters) was redistilled until the last portion of the distillate contained no halogen. The acetone fraction was redistilled in a column and yielded 2 g of chloroacetone. The water distillate gave 2.3 g of 2-methyl-6-chlorobenzthiazole, m.p. 79-80°. Cinnamic acid which precipitated in the distillation flask when it cooled, was separated from the brown mass which was dissolved in chloroform and the solution chromatographed on aluminum oxide. The eluate from the first zone (light yellow in color) was collected separately, and the chloroform was completely distilled from it. It gave 4.5 g of base. The eluate from the second zone (dark brown in color) was partly freed from chloroform by distillation; the solution was repeatedly chromographed. It yielded 2.7 g of base. The total yield was 7.2 g (28%), m.p. 109-111°. The base was recrystallized twice from alcohol using animal charcoal. Yield 4.3 g (17%). Light-yellow plates with a pearly luster; m.p. 118°.

Found %: S 13.01, 13.03; N 5.50, 5.76. $C_{16}H_{13}NS$. Calculated %: S 12.71; N 5.57.

2-Methyl-6-styrylbenzthiazole from styrene. 8.2 g 2-methyl-6-aminobenzthiazole was diazotized as described above. A mixture of 5.5 g of styrene (stabilized with 0.5% hydroquinone), 50 ml of acetone, and 15.3 g of sodium acetate was cooled to −2°. To the mixture was added the diazonium chloride solution and 1 g of cupric chloride in 3 ml of water. Stirring continued for 2 hours during which time the temperature was raised to 35° and then the mixture was stirred for another 3 hours at 35°. The solution was filtered, the acetone layer was separated, and the acetone was distilled with steam. To the residue was added 40 g of potassium hydroxide in 100 ml of alcohol, and the mixture was boiled for 2 hours. Then the solution was steam distilled to remove 2-methyl-6-chlorobenzthiazole and unreacted styrene. The residual dark mass was extracted with chloroform and the solution was chromatographed on aluminum oxide. We obtained light-yellow crystals which were recrystallized from alcohol. The yield was 0.5 g (4%), m.p. 118°. The mixed melting point with the 2-methyl-6-styrylbenzthiazole described above gave no depression.

2-Methyl-6-(p-methoxystyryl)-benzthiazole. 16.4 g of 2-methyl-6-aminobenzthiazole was diazotized in the usual way. A mixture of 17.8 g p-methoxycinnamic acid, 200 ml of acetone, 24 g of sodium acetate, and 5.1 g of cupric chloride in 10 ml of water was cooled to −7° and the solution of diazonium chloride was added to it during 40-45 min. The reaction mixture was stirred 5-6 hours while the temperature was slowly raised to 20°; acetone and 2-methyl-6-chlorobenzthiazole (1.2 g) were distilled off with steam. After decantation of the water solution, from which as it cooled, had precipitated 1.5 g of p-methoxycinnamic acid, we obtained 29.4 g of a dark brown residue. The product was ground and dissolved in 400-500 ml of chloroform, from which cooling precipitated 5.5 g of p-methoxycinnamic acid. The chloroform was partly distilled off and the residue was submitted to chromatography. We obtained 2.4 g of red-brown substance which was twice recrystallized from alcohol with animal charcoal. Yield 1.9 g (6.8%). Silvery scales with a greenish tint; m.p. 170-171°. The yield based on reacting p-methoxycinnamic acid was 11.1%.

Found %: N 5.19, 5.32; S 11.34, 11.45. $C_{17}H_{15}ONS$. Calculated %: N 4.98; S 11.39.

2-Methyl-6-(α-thienylvinyl)-benzthiazole. 16.4 g of 2-methyl-6-aminobenzthiazole was diazotized as described above. A mixture was prepared of 15.4 g 2-thienylacrylic acid, 250 ml of acetone, 24 g of sodium acetate, and 5.1 g of cupric chloride in 10 ml of water. Addition of diazonium chloride and stirring were carried out as above. The acetone and 2-methyl-6-chlorobenzthiazole (0.3 g) were steam-distilled as above. From the distillation flask after decantation of the water layer we obtained 30.4 g of dark product and 2.2 g of thienylacrylic acid. The product was ground, dissolved in 500 ml of chloroform, filtered, the solution concentrated to 70-80 ml, and twice chromatographed on aluminum oxide. We obtained 3.8 g of base which was twice recrystallized from alcohol. Yield 2.45 g (9.5%). Glittering golden scales with m.p. 119-120°.

Found %: N 5.22, 5.45; S 24.78, 24.69. $C_{14}H_{11}NS_2$. Calculated %: N 5.45; S 24.90.

Ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole. 2.51 g of 2-methyl-6-styrylbenzthiazole and 4 g of ethyl p-toluene sulfonate were heated on an oil bath for 12 hours at 150-160°. The salt was dissolved in boiling water, the water solution was washed with benzene, decolorized with animal charcoal, evaporated on the water bath, and heated to 120-125°. Yield 4.3 g (94%). For the synthesis of dyes the salt was used without further purification.

Ethyl p-toluene sulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole. 0.56 g of 2-methyl-6-(p-methoxystyryl)-benzthiazole and 0.6 g of ethyl p-toluenesulfonate were heated 10 hours at 150-160°. The yield of salt was quantitative.

Ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole. 1 g of 2-methyl-6-(α-thienylvinyl)-benzthiazole and 1.2 g of ethyl-p-toluenesulfonate were heated 10 hours at 140-150°. Yield 1.7 g (96%).

Dyes

3,3'-Diethyl-6,6'-distyrylthiacarbocyanine iodide (I). A mixture of 1.3 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 1.3 g of orthoformic ester, and 8 ml of pyridine was boiled 30 min and poured into a hot aqueous solution of potassium iodide. The dye was filtered, washed with warm water,

dissolved in 50 ml of pyridine, filtered, and to the hot solution was added 75 ml of boiling alcohol. The crystals which precipitated were separated and washed with alcohol and ether. Yield 0.34 g (34%). The bronze crystals melted 234-235°.

Found %: I 18.03, 18.06. $C_{37}H_{33}N_2S_2I$. Calculated %: I 18.24.

3,3'-Diethyl-9-methyl-6,6'-distyrylthiacarbocyanine bromide (II). 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.5 g of orthoacetic ester, and 3 ml of pyridine were boiled 35 min. The dye was precipitated by potassium bromide and crystallized from alcohol. Yield 0.1 g (30%). The crystals had a steely color; m.p. 272°.

Found %: Br 11.96, 11.62. $C_{38}H_{35}N_2S_2Br$. Calculated %: Br 12.06.

3,3',9-Triethyl-6,6'-distyrylthiacarbocyanine bromide. (III). A mixture of 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.5 g of orthopropionic ester, and 2 ml of pyridine was boiled 20 min. The dye was precipitated by potassium bromide. The thick, non-crystalline mass was washed with water and allowed to stand until the next day. The precipitate of the dye was filtered and twice crystallized from alcohol. Yield 0.16 g (48%). Glittering dark-green tablets; m.p. 199-200°.

Found %: Br 11.52, 11.50. $C_{39}H_{37}N_2S_2Br$. Calculated %: Br 11.81.

3,3'-Diethyl-6,6'-di-(p-methoxystyryl)-thiacarbocyanine bromide (IV). To a solution of 0.96 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole in 5 ml of pyridine was added 1 g of orthoformic ester and 5 drops of acetic anhydride; the mixture was boiled 30 min. The dye was precipitated by ether, dissolved in alcohol and converted to the bromide by the action of an alcoholic solution of potassium bromide. The bromide of the dye was filtered, washed with hot water, alcohol, and ether. Yield 0.48 g (71%). Dark-green crystals; m.p. 217°.

Found %: Br 11.12, 10.95; S 9.12, 9.30. $C_{39}H_{37}O_2N_2S_2Br$. Calculated %: Br 11.28; S 9.03.

3,3',9-Triethyl-6,6'-di-(p-methoxystyryl)-thiacarbocyanine iodide (V). A mixture of 0.96 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole, 1 g of orthopropionic ester, and 3 ml of pyridine was boiled for 35 min. The dye was precipitated by potassium bromide. After crystallization from alcohol the fine crystals weighed 0.24 g, and for further purification were dissolved in 50 ml of alcohol and precipitated by aqueous alcoholic solution of potassium iodide. After recrystallization from alcohol the crystals weighed 0.11 g (14%). Fine violet-black crystals; m.p. 243-244°.

Found %: I 15.87, 15.22. $C_{41}H_{41}O_2N_2S_2I$. Calculated %: I 16.20.

3,3'-Diethyl-6,6'-di-(α-thienylvinyl)-thiacarbocyanine bromide (VI). To a solution of 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole in 4 ml of pyridine was added 1 g of orthoformic ester and 5 drops of acetic anhydride. The mixture was boiled 20 min. The dye was precipitated by potassium bromide, crystallized from alcohol and then from glacial acetic acid. Yield 0.27 g (41%). Green crystals; m.p. 215°.

Found %: Br 12.07, 12.13. $C_{33}H_{29}N_2S_4Br$. Calculated %: Br 12.10.

3,3',9-Triethyl-6,6'-di-(α-thienylvinyl)-thiacarbocyanine bromide (VII). This was obtained in an analogous way from 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole and 1 g of orthopropionic ester. The dye was twice recrystallized from alcohol. Yield 0.25 g (36%). Green crystals; m.p. 199°.

Found %: Br 10.97, 11.08. $C_{35}H_{33}N_2S_4Br$. Calculated %: Br 11.61.

[3-Ethyl-4,5-benzobenzthiazole-2)] - [3-ethyl-6-styrylbenzthiazole-(2)]-trimethinecyanine iodide. (VIII). 0.45 g of ethyl p-toluene sulfonate of 2-methyl-6-styrylbenzthiazole and 0.54 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole were dissolved in 5 ml of pyridine. To the solution was added 1 ml of acetic anhydride and the mixture was boiled for 20 min. The dye was precipitated by potassium iodide and crystallized from a mixture of 60 ml of alcohol and 10 ml of pyridine. Yield 0.2 g (31%). Green crystals; m.p. 208° (with decomposition).

Found %: I 19.77, 19.67. $C_{33}H_{29}N_2S_2I$. Calculated %: I 19.72.

[3-Ethyl-4,5-benzobenzthiazole-(2)] - [3-ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-trimethinecyanine iodide (IX). To a solution of 0.48 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole in 10 ml of pyridine was added 0.54 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole and 1 ml of acetic anhydride. The mixture was boiled for 20 min. The dye was precipitated with potassium bromide, dissolved in chloroform, and chromatographed on aluminum oxide. The column was washed with ether. The dye was removed by methanol from the upper zone (dark blue) and was then precipitated by potassium bromide, dissolved in 40 ml of 50% acetic acid. The dark-green crystals melted at 181-183° (with decomposition).

Found %: I 18.75, 19.04. $C_{34}H_{31}ON_2S_2I$. Calculated %: I 18.84.

[3-Ethyl-4,5-benzobenzthiazole-(2)] - [3-ethyl-6-(α-thienylvinyl benzthiazole-(2)]-trimethinecyanine iodide (X). This was obtained in an analogous way from 0.48 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-4,5-benzobenzthiazole and 0.51 g of ethyl p-toluenesulfonate of 2-methyl-6-(α-thienylvinyl)-benzthiazole. The dye was purified as described above and was crystallized from nitromethane. Yield 0.1 g (17%). Violet black crystals; m.p. 196°.

Found %: I 19.74, 19.69. $C_{31}H_{27}N_2S_3I$. Calculated %: I 19.54.

[3-Ethyl-5-methoxybenzthiazole-(2)] - [3-ethyl-6-styrylbenzthiazole-(2)]-trimethinecyanine iodide (XI). A mixture of 0.45 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole, 0.52 g of ethyl 1 p-toluenesulfonate of 2-β-acetanilidovinyl-5-methoxybenzthiazole, 4 ml of pyridine, and 1 ml of acetic anhydride was boiled for 30 min. The dye was precipitated by potassium bromide, dissolved in alcohol, and transformed into the iodide. After it was crystallized from alcohol, the yield was 0.24 g (38%); m.p. 252°.

Found %: I 19.82, 19.77. $C_{30}H_{29}ON_2S_2I$. Calculated %: I 20.35.

[3-Ethyl-5-methoxybenzthiazole-(2)] - [3-ethyl-6-(p-methoxystyryl)-benzthiazole-(2)]-trimethinecyanine iodide (XII). This was obtained in an analogous way from 0.48 g of ethyl p-toluene sulfonate of 2-methyl-6-(p-methoxystyryl) benzthiazole and 0.52 g of ethyl p-toluenesulfonate of 2-β-acetanilidovinyl-5-methoxybenzthiazole. Yield 0.27 g (41%). Fine green crystals; m.p. 259°.

Found %: I 18.40, 18.30. $C_{31}H_{31}O_2N_2S_2I$. Calculated %: I 19.42.

3,3'-Diethyl-6'-styryl-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden -2"-α-phenylethylidene)-thiazolinothiacyanine p-toluenesulfonate (XIII). 0.95 g of 3-ethyl-5-(3'-ethyl-6',7'-tetramethylenebenzthiazolinyliden-2'-α-phenylethylidene)-thiazoliden-2-thione-4-one* and 1 g of dimethyl sulfate were heated on an oil bath for 25 min at 120°. After cooling, the quaternary salt was dissolved in 8 ml of pyridine and 0.9 g of ethyl p-toluenesulfonate of 2-methyl-6-styrylbenzthiazole was added and the mixture was heated 1 hour and 15 min at 120°. The precipitated rhodacyanine was filtered, and washed with methanol and ether. Yield 1.35 g (75%). Glittering green crystals; m.p. 303° (with decomposition).

Found %: S 15.07, 14.98. $C_{51}H_{49}O_4N_3S_4$. Calculated %: S 15.43.

0.5 g of the rhodacyanine (XIII) was dissolved in 230 ml of alcohol, the solution was filtered, the rhodacyanine was precipitated by potassium bromide and washed with hot water, methanol, and ether. Yield 0.3 g (68%). Glittering green tablets; m.p. 287° (with decomposition).

Found %: Br 9.98, 9.89. $C_{44}H_{42}ON_3S_3Br$. Calculated %: Br 9.95.

3,3'-Diethyl-6'-(p-methoxystyryl)-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden-2"-α-phenylethyliden)-thiazolinothiacyanine iodide (XIV). 0.6 g of merocyanine and 1 g of dimethyl sulfate were heated 25 min at 115-120°. To the pyridine solution of the quaternary salt of merocyanine was added 0.6 g of ethyl p-toluenesulfonate of 2-methyl-6-(p-methoxystyryl)-benzthiazole. The mixture was heated 1 hour 15 min at 120-125°. The rhodacyanine was precipitated by ether, dissolved in chloroform, and chromatographed on aluminum oxide. (It was necessary to protect the chromatographic column from the action of direct sunlight.) The column was washed with chloroform and acetone, and the rhodacyanine was eluted with methanol. The methanol was partly distilled off and the filtered solution was treated with an aqueous alcoholic solution of potassium iodide. The dye was washed with water, alcohol, and ether. Yield 0.43 g (39%). Green crystals with a bronze glint; m.p. 284°.

*For the sake of brevity, this preparation will hereafter be called "merocyanine".

Found %: I 13.87, 13.98. $C_{45}H_{44}O_2N_3S_3I$. Calculated %: I 14.41.

3,3'-Diethyl-6'-(2-thienylvinyl)-4-keto-5-(3"-ethyl-6",7"-tetramethylenebenzthiazolinyliden-2"- α-phenylethyliden)-thiazolinothiacyanine iodide (XV). 0.95 g of merocyanine and 1 g of dimethyl sulfate were heated 20 min at 120-125°. After cooling, the quaternary salt was dissolved in pyridine, and to the solution was added 0.92 g of ethyl p-toluenesulfonate of 2-methyl-6-(2'-thienylvinyl)-benzthiazole. The mixture was heated 1 hour and 15 min at 120-125°, the rhodacyanine was precipitated by 30 ml of methanol, washed with ether, and purified as described above. The dye was precipitated by potassium iodide, and washed with water, methanol, and ether. Yield 0.41 g (24%). Green crystals; m.p. 294°.

Found %: I 14.78, 14.80. $C_{42}H_{40}ON_3S_4I$. Calculated %: I 14.82.

SUMMARY

1. We obtained three new bases by the action of diazotized 2-methyl-6-aminobenzthiazole on acrylic acids: 2-methyl-6-styrylbenzthiazole, 2-methyl-6-(p-methoxystyryl)-benzthiazole, and 2-methyl-6-(α-thienylvinyl)-benzthiazole.

2. From these bases and ethyl p-toluenesulfonate, we synthesized the quaternary salts which contain unsaturated substituents in the 6-position of benzthiazole.

3. By condensation of the quaternary salts with ortho esters and intermediary compounds we obtained 7 symmetrical thiacarbocyanines, 5 unsymmetrical thiacarbocyanines, and 3 rhodacyanines, which contained unsaturated groups in the benzthiazole nucleus.

4. We showed that the introduction of unsaturated substituents in position 6 of the cyanine dye molecules shifted the absorption maxima sharply in the long wave portion of the spectra.

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MONOANILS OF GLUTACONIC ALDEHYDE

I. DERIVATIVES OF PRIMARY AROMATIC AMINES

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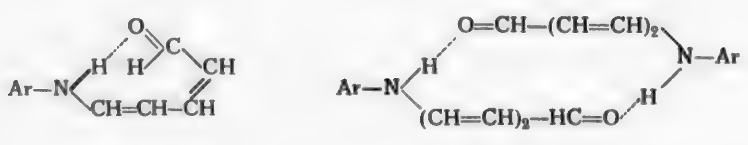
By treatment of pyridine 2,4-dinitrochloroarylates with alkali, Zincke [1] obtained red compounds which readily formed hydrazones and condensed with primary aromatic amines. He considered it probable that they had a structure with an open pentamethine chain formed as a result of fission of the pyridine ring. He ascribed a similar structure to the compounds obtained by treatment of N-substituted pyridine dyes with alkali [2]. These compounds are known under the name of "Zincke aldehydes"; they are described also in the works of other authors [3]. Of the primary-amine derivatives, only dinitro-substituted ones were known [1]. The corresponding derivatives of aniline [4] and other primary aromatic amines [5] were prepared by one of us. However, the nature of these compounds was not investigated in detail, since they were obtained in low yields. For the purpose of making a more thorough study of similar compounds we developed a method of preparation of derivatives of aniline and other amines, achieving considerable yields in some cases, and determined their capacity for condensation with aromatic amines and with compounds containing active methyl groups.

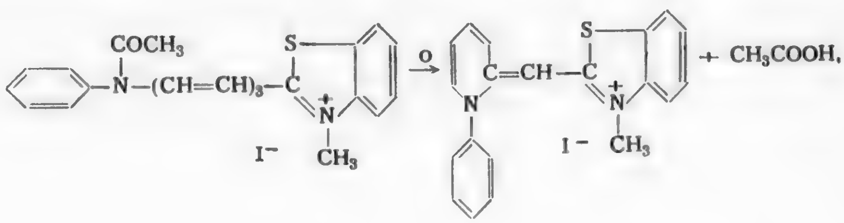
By analogy with known Zincke aldehydes we considered the compounds which we obtained to be monoanils of glutaconic aldehyde; however, unlike Zincke aldehydes, they do not condense with primary aromatic amines under similar conditions, and they form hydrazones with difficulty. We carried out the condensation of the monoanils with aromatic amines under varied conditions: in acetic acid in the presence of hydrochloric acid, in acetic anhydride in the presence of hydrogen chloride, and in pyridine in the presence of hydrogen chloride. In the last case only, a color change was observed, which could be used as an indication of reactions taking place. On reaction of the unsubstituted monoanil with aniline hydrochloride in pyridine a pronounced deepening of color occurred; a red, crystalline substance was obtained, which proved to be the monoanil hydrochloride. A similar substance was obtained on reaction of p-anisidine hydrochloride with the unsubstituted monoanil. Monoanils which were derivatives of other amines exhibited similar behavior, but their hydrochlorides were very hygroscopic and were not isolated. Therefore, in the reaction of monoanils with amine hydrochlorides in pyridine, transfer of hydrogen chloride from the amine to the monoanil is all that occurs; we were not able to obtain the expected mixed pentamethine dye in a single case [6]. Secondary aromatic amines did not react with the monoanils under investigation, either.

The negative results of the attempts at condensation of glutaconic aldehyde monoanils with aromatic amines is difficult to explain if it is assumed that they contain a free carbonyl group. Furthermore, glutaconic aldehyde monoanils, like other carbonyl compounds [7], deepen in color in the presence of acids. Spectroscopic investigations of glutaconic aldehyde monoanils showed that they are amphoteric compounds; the dual reactivity and the possibility of formation of a hydrogen bond (which may be either intra- or intermolecular) apparently cause inertness of the carbonyl group in these compounds in certain reactions. Dinitro-substituted

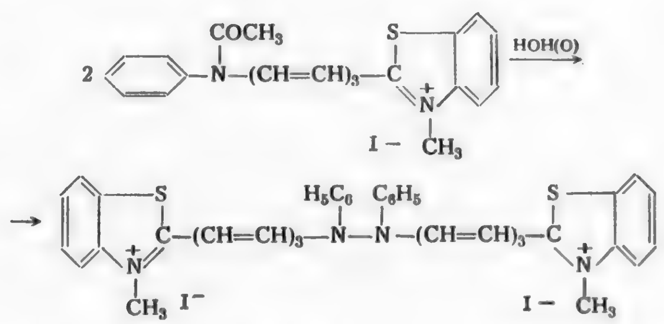


monoanils apparently have little tendency toward similar conversions, owing to the ortho-effect between the nitro and amino groups.

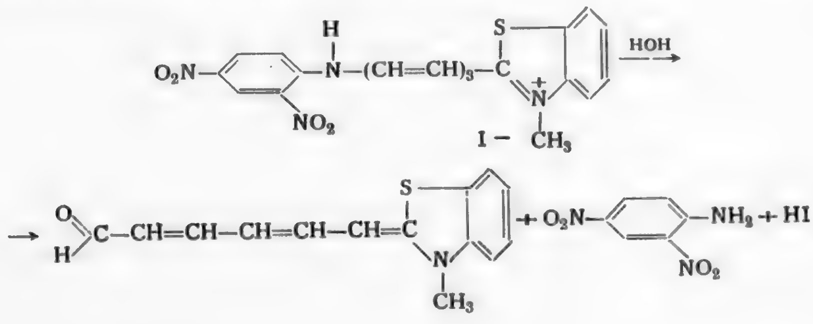
The capacity of the monoanils obtained by us for condensation with compounds containing active methyl groups may serve as an indirect proof of their structure. We carried out the condensation of the unsubstituted monoanil, and also the p-methyl-p-methoxy- and 2,4-dinitromonoanils, of glutaconic aldehyde with 2,3-dimethylbenzothiazolium iodide under varying conditions. The first three monoanils formed red-violet dyes as end-products; in the case of the aniline derivative an intermediate blue dye was obtained. The violet dyes and the intermediate blue dye react differently to acid; the violet dyes are decolorized on addition of excess acid, whereas the color of the blue dye is not visibly changed. The heightening of the color on heating suggests the hypothesis that a mixed hexamethine dye (hemicyanine) is formed at first and is then acetylated on heating; however, analytical data do not confirm this hypothesis. The low yields of the dyes and their color suggest that the hexamethine dye initially formed undergoes oxidative condensation with the formation either of an unsummetrical pyridocyanine,



or of a bisazomethine dye



On condensation of the 2,4-dinitromonoanil with 2,3-dimethylbenzothiazolium iodide a yellow-brown substance was obtained, which contained neither the dinitrophenyl radical nor halogen. It is possible that the hexamethine dye first formed decomposes according to the scheme



Although the nature of the products of condensation of glutaconic aldehyde monoanils with 2,3-dimethylbenzothiazolium iodide has not been finally established (further investigation is required), the experiments which have been done show that under corresponding conditions glutaconic aldehyde monoanils are capable of reactions characteristic of carbonyl compounds.

EXPERIMENTAL

In order to increase the yields of glutaconic aldehyde monoanils we made certain changes in the method developed earlier [8]. After addition of a 15% excess of sodium hydroxide solution to a concentrated arylpyridinium chloride solution (until yellow material ceased to appear at the point where a drop of the alkali solution fell), the mixture was heated in a water bath at 60-70° until the initially formed resin crystallized and the pseudobase was entirely converted to the monoanil (5-10 minutes). The characteristics of the glutaconic aldehyde monoanils investigated by us are given in Table 1.

TABLE 1

Glutaconic Aldehyde Monoanils

Name of compound	Yield (%)	Melting point	Color of crystals	Empirical formula	Nitrogen content (in %)	
					calc.	found
1-(Phenylamino)-pentadien-1,3-al-5 [4]	74	171°	Red-violet	$C_{11}H_{11}ON$	8.09	8.12
1-(p-Methylphenylamino)-pentadien-1,3-al-5[4]	79	176	Brown-red(from benzene	$C_{12}H_{13}ON$	8.00	8.05
1-(p-Methoxyphenylamino)-pentadien-1,3-al-5	60	165	Red (from acetone)	$C_{12}H_{13}O_2N$	7.30	7.38
1-(p-Biphenylamino)-pentadien-1,3-al-5			Red (from acetone)	$C_{17}H_{15}ON \cdot {}^1/_2C_2H_6O$	5.03	5.16
1-(α-Naphthylamino)-pentadien-1,3-al-5	65	207	Orange (from benzene)	$C_{15}H_{13}ON$	6.28	6.44
1-(β-Naphthylamino)-pentadien-1,3-al-5	65	201	Red-brown from benzene)	$C_{15}H_{13}ON$	6.28	6.35
1-(2,4-Dinitrophenylamino)-pentadien-1,3-al-5 [1]	90	159	Red (from dichloroethane)	$C_{11}H_9O_5N_3$	15.97	15.86

The condensations of the unsubstituted monoanils of glutaconic aldehyde with aniline and p-anisidine hydrochlorides were carried out with equimolar proportions in the cold. Thus, for instance, to a thoroughly ground mixture of 0.6 g of the monoanil and 0.4 g of aniline hydrochloride was added 5 ml of pyridine. In this case the solution turned red-violet, and after a few minutes a precipitate formed. After washing with ether and drying, the precipitate weighed 0.38 g. M. p. 112°.

Found %: N 6.70, 6.62. $C_{11}H_{11}ON \cdot HCl$. Calculated %: N 6.68.

On treatment of an aqueous solution of the red substance with alkali, the original monoanil was obtained.

Condensation of 2,3-dimethylbenzothiazolium iodide with glutaconic aldehyde monoanils. The condensation of 2,3-dimethylbenzothiazolium iodide and the monoanil in equimolar quantities was carried out in acetic anhydride (5 ml for 1 g of the mixture). The mixture was heated on a grid for 40-50 minutes (until a stable, unchanging color appeared) and left for 12 hours. The crystals which had separated out were then washed in the filter with ether and water and were recrystallized (Table 2).

TABLE 2

Products of Condensation of 2,3-Dimethylbenzothiazolium Iodide with Glutaconic Aldehyde Monoanils

Amine, the derivative of which is the monoanil brought into condensation	Duration of the condensation (in min)	Melting point	Color of crystals (solvent)	Absorption maximum (λ_{max}) in ethanol (in $m\mu$)	Assumed empirical formula	Nitrogen content (in %)	
						calc.	found
Aniline	40	339°	Violet (from alcohol)	565	$C_{20}H_{17}N_2SI$	6.31	6.49
Aniline	8	—	Golden-green from alcohol)	648*	$C_{22}H_{21}ON_2SI$ / $C_{23}H_{21}N_2S_2I$	5.76 / 5.43	5.47
p-Toluidine . .	40	240	Green (from dichloroethane)	562	$C_{21}H_{18}N_2SI \cdot C_2H_4Cl_2$	5.03	4.87
p-Anisidine . .	40	—	Violet (from alcohol	560	$C_{21}H_{21}ON_2SI$	5.88	5.96
2,4-Dinitroaniline	50	259	Brown (from glacial acetic acid)	—	$C_{14}H_{13}ONS$	5.76	5.70

SUMMARY

1. Glutaconic aldehyde monoanils which are derivatives of primary aromatic amines have been investigated.

2. It has been shown that neither the unsubstituted monoanil of glutaconic aldehydes nor those which contain electron-donor substituents in the aromatic rings condense with aromatic amines.

3. The condensation of several monoanils with 2,3-dimethylbenzothiazolium iodide has been carried out; condensation products were obtained, the structure of which has not been definitely established. Hypotheses on the structure of the products obtained are stated.

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*For the coresponding non-acylated hexamethine dye, the absorption maximum in ethyl alcohol is given a 613 $m\mu$ [9].

**Original Russian pagination. See. C.B. Translation.

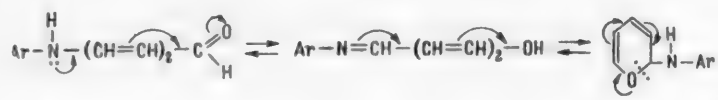
MONOANILS OF GLUTACONIC ALDEHYDE

II. EFFECT OF THE MEDIUM ON THE COLOR OF DERIVATIVES OF PRIMARY AROMATIC AMINES

N. E. Grigor'eva and I. K. Gintse

The question of the effect of the medium on the color of organic compounds has long received the attention of investigators studying questions of color. Non-saltlike, internally ionized dyes are especially sensitive to change in the medium. Their susceptibility to change in color on transition from solvent to solvent has long been known, and various hypotheses explaining this phenomenon have been proposed [1-5]. The hypothesis, first advanced by A. I. Kiprianov andco-workers [6] (and later by other authors [7]), of the dependence of the color change in internally ionized dyes on the polarity of the solvent has been widely accepted by organic chemists. Depending on the character of the color change, A. I. Kiprianov andco-workers divide internally ionized dyes into three types: those the color of which is deepened as the dielectric constant of the solvent decreases (Type I), those the color of which is heightened under these conditions (Type II), and those which occupy an intermediate position.

Those glutaconic aldehyde monoanils which are derivatives of primary aromatic amines are tautomeric compounds, the structure of which may be expressed by several formulas



These compounds belong to the class of internally ionized compounds, and each of the given forms may be represented as a dipolar ion. Compounds of this type are very sensitive to a change of medium – they change color in various "neutral" solvents in the presence of acids or alkalis.

Unlike the internally ionized compounds investigated earlier [6, 7], no definite dependence between the color change and the polarity of the solvent is observed in the case of glutaconic aldehyde monoanils. The peculiarities in the structure of these compounds and the variations of their color in different media were grounds for a more thorough investigation of them for the purpose of elucidating the factors which affect the change of absorption of internally-ionized compounds. The relatively good solubility of the monoanils permitted investigation of their absorption spectra in many organic solvents; the spectra of the unsubstituted monoanils in solvent mixtures were also investigated. The absorption spectra of seven monoanils derived from primary amines and, for comparison, a methylaniline derivative were determined in neutral, acid, and alkaline media.

Discussion of absorption spectra. On comparison of the absorption maxima of glutaconic monoanils (Table 1) in a single solvent, e.g., butyl alcohol, it is evident that the character of the aromatic radical has a considerable effect on the variation in color of the monoanils. As the basicity of the amino radical decreases, the color of the monoanil is heightened; the 2,4-dinitroaniline derivative (VII) is the most "highly" colored. Unlike the absorption spectra of other derivatives of primary aromatic amines, that of the 2,4-dinitromonoanil varies little from solvent to solvent; the tendency toward displacement of the absorption maximum toward the long-wave part of the spectrum is noticeable only in strongly polar solvents. Comparison of the data of

TABLE 1

Absorption Maxima (in mμ) of Glutaconic Aldehyde Monoanils of the Type $Ar{-}\overset{H}{\overset{|}{N}}{-}(CH{=}CH)_2{-}C\overset{O}{\underset{H}{\lessgtr}}$ in Various Solvents (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

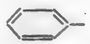
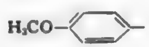
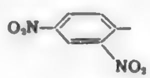
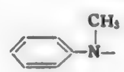
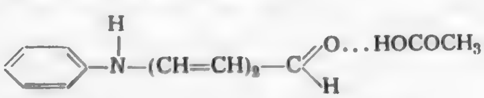
No. of compound	Ar	Alcohol			Acetone	Pyridine	Dichloro-ethane	Acetic acid	Dioxane	Benzene	Bromo-benzene	Nitro-benzene
		methyl	ethyl	n-butyl								
(I)		440 (1.8)	442 (1.9)	445 (1.8)	471 (2.5)	480 (2.3)	462 (1.74)	495 (2.9)	508 (1.5)	485 (1.9)	480	515 (0.68)
(II)		442 (1.5)	446 (1.8)	452 (1.6)	475 (2.5)	482 (2.1)	461 (1.2)	500 (2.6)	Red	486 (1.6)	—	523 (1.8)
(III)		—	450 (1.8)	452 (1.5)	474 (1.9)	482 (1.8)	462	492 (1.3)	—	486 (1.4)	—	532
(IV)		—	—	450 (0.7)	—	495 (1.2)	—	509 (1.5)	472	495 (1.2)	—	—
(V)		430 (2.1)	435 (2.0)	446 (1.8)	471 (2.6)	481 (2.5)	460 (1.2)	494 (1.3)	—	483 (1.9)	—	505; 470 (1.3)
(VI)		450 (0.5)	455 (1.9)	462 (1.8)	483 (1.4)	500 (1.9)	475 (1.3)	509 (3.0)	Red	497 (2.0)	—	530; 520 (0.76)
(VII)		—	397 (3.2)	387 (2.2)	—	—	387 (3.0)	387 (3.0)	—	—	—	442 (1.8)
(VIII)		—	380 (6.3)	380 (4.3)	367 (5.4)	380 (4.0)	350 (3.0)	390 (3.4)	—	367 (3.8)	—	—

Table 1 shows that in alcohols the displacement of the absorption maximum for compounds (I) – (VIII) is slight, although the polarity of the alcohols varies. The color is noticeably deeper in acetone (displacement of maximum, 20-26 mμ toward the long-wave end), whereas the polarity of the latter is only slightly greater than that of butyl alcohol. If the color change of monoanil (I) is followed thru 11 solvents, no definite dependence between the color change and the polarity of the solvent can be established; the color change varies, depending on the choice of solvent. For instance, in a series of solvents: alcohols, dichloroethane, bromobenzene, benzene, and dioxane the color is deepened as the dielectric constant of the solvent decreases (Type I). In such solvents as nitrobenzene, acetone, and dichloroethane the color is heightened as the polarity of the solvent decreases (Type II). In the series methyl alcohol – dichloroethane (excepting acetone) this compound may be referred to the intermediate type, as regards color change. Apparently no dependence can be established between the variation in the dipole moment of the solvent and the color of the monoanil; thus the color of a benzene solution of monoanil (I) differs little from that of a pyridine solution, although the dipole moments of these solvents are quite different.

The variation in the absorption of monoanil (I) in solvent mixtures is shown in Table 2. The monoanil was dissolved in a definite volume of one solvent, and the solution was then diluted with a second solvent; the spectra of the solutions were determined when the latter were freshly prepared and again, one day later. As is evident on comparison of the data given in Table 2, dilution of the alcoholic solution with acetone does not affect the light absorption; the latter is the same as in the alcoholic solution. Dilution of the acetone solution with alcohol markedly changes the absorption, and the latter approaches the absorption of the alcoholic solution. It is quite obvious that in the reaction of the monoanil with the alcohol a compound (complex) is formed, more stable than that formed in the reaction of the monoanil with acetone. The stability of the complexes is probably due to the difference in basicity between the alcohol and acetone. The variation in the absorption of solutions in alcohol – pyridine mixtures is even more pronounced. These solvents differ markedly in basicity; if the monoanil reacts with the alcohol as a base, then it acts as an acid in pyridine. In alcohol – benzene mixtures the absorption is only slightly dependent on the solvent ratio and the order of solution of the monoanil. It is scarcely probable that the monoanil would react with benzene; obviously, in benzene solution the light is absorbed by neutral monoanil molecules. The absorption of the monoanil in alcohol-benzene solution is due mainly to the monoanil-alcohol complex; this complex does not dissociate even when the alcoholic solution is greatly diluted (25 : 75). In pyridine–benzene mixtures, regardless of the solvent ratio, the absorption approximates that of a pyridine solution; after a day the absorption maximum coincides with the additive one.

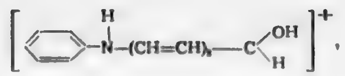
The variation in the absorption of solutions of monoanil (I) in mixtures of two solvents clearly shows that this absorption is not connected with the polarity of the solvents (since, when the ratios are the same, the polarity is the same). The absorption depends on which of the solvents was the first wherein the monoanil was dissolved; i.e., it depends on the structure and stability of the monoanil–solvent complex.

On comparison of the absorption curves of monoanil (I), shown in Figure 1, variations in the spectra, depending on the nature of the solvents, are clearly evident. The great difference between the spectra of the monoanil in butyl alcohol and in acetic acid is due not to the difference in polarity between these solvents, but mainly to the structure of the compounds formed by the monoanil with the solvents. Acetic acid is a weak acid, and mainly undissociated molecules react with the monoanil. The attachment of the acid to the carbonyl group oxygen causes halochromic deepening of the color [8].



The acid may be attached also to the amino group of the monoanil.

In this case "deactivation" of the auxochrome leads to heightening of the color, and the band with maximum at 375 mμ possibly belongs to the ammonium salt. After diluting the acetic acid solution with butyl alcohol a deepening of the color is observed. The intensity of the bands in the visible and near-ultraviolet regions decreases (the monoanil concentration being the same throughout), but the absorption in the farther ultraviolet becomes more pronounced. The increase in the polarity of the solution, observed after diluting with butyl alcohol, increases the degree of dissociation of the acetic acid [9] and facilitates the formation



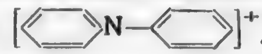
of the carbonium salt which causes the deepening of the color. The carbonium salt is not stable; a molecule of water is easily split off from it with formation of the corresponding pyridine salt: .
This process takes place more rapidly when the alcoholic solution is diluted with acetic acid.

TABLE 2

Absorption Maxima (in mμ) of Glutaconic Aldehyde Monoanil (I) in Solvent Mixtures (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

Solvent mixtures	Ratio (in vol. %)	Absorption in mixtures: immediately after mixing	Absorption in mixtures: 24 hours later *	Additive absorption
Alcohol–acetone	75 : 25	442 (1.90)	—	
	50 : 50	443 (1.88)	—	
	25 : 75	443 (1.98)	—	
Acetone–alcohol	25 : 75	443 (1.98)	—	456.5 (2.05)
	50 : 50	443 (1.83)	—	
	75 : 25	455 (1.90)	455 (1.80)	
Alcohol–pyridine	75 : 25	445 (1.90)	445 (1.80)	
	50 : 50	450 (1.80)	450 (1.88)	
	25 : 75	452 (1.86)	465 (1.90)	
Pyridine–alcohol	25 : 75	445 (1.90)	445 (1.90)	461 (2.08)
	50 : 50	471 (1.78)	450 (1.90)	
	75 : 25	473 (2.3)	468 (1.93)	
Alcohol–benzene	75 : 25	445 (1.88)	445 (1.83)	
	50 : 50	448 (1.95)	448 (1.78)	
	25 : 75	448 (1.67)	458 (1.72)	
Benzene–alcohol	25 : 75	445 (1.75)	445 (1.95)	463.5 (1.83)
	50 : 50	448 (1.81)	448 (1.90)	
	75 : 25	465 (1.69)	470 (1.74)	
Pyridine–benzene	75 : 25	480 (2.16)	482 (2.14)	
	50 : 50	481 (2.16)	482 (2.14)	
	25 : 75	481 (2.05)	483 (2.07)	
Benzene–pyridine	25 :75	480 (2.05)	482 (2.14)	482.5 (2.00)
	50 :50	481 (2.16)	482 (2.14)	
	75 :25	481 (2.05)	483 (2.07)	

Deepening of the color in the presence of acids is observed in the cases of monoanils (I)–(VI), the color changing considerably on transition from solvent to solvent (Table 1). For instance, the absorption maximum of monoanil (I) in the presence of hydrogen chloride is displaced toward the long-wave end in such solvents as acetone (501 mμ), butyl alcohol (510 mμ), dichloroethane (525 mμ), and benzene (536 mμ). In the presence of acid the less polarity the solvent has, the deeper and more stable the color is. In more polar solvents – methyl and ethyl alcohols – the solutions are instantly decolorized in the presence of hydrogen chloride. These facts confirm the above-stated explanation of the change in monoanil spectra in an acid medium.

The change in color of monoanils derived from primary amines takes place in time in the presence of alkali. The change in absorption of monoanil (I) is shown in Table 3.

The deepening of the color in the presence of alkali is due to tautomeric conversion; the sodium enolate is formed at a varying rate depending on the basicity of the monoanil, and the stabilities of the salts are unequal.

*The spectra of monoanil (I) in the individual solvents were unchanged one day later.

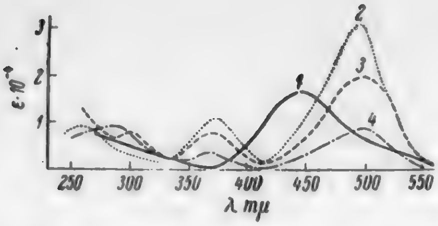


Fig. 1. Absorption spectra of monoanil (I). 1) In n-butyl alcohol; 2) in glacial acetic acid; 3) in acetic acid + 50% n-butyl alcohol; 4) in n-butyl alcohol + 50% acetic acid.

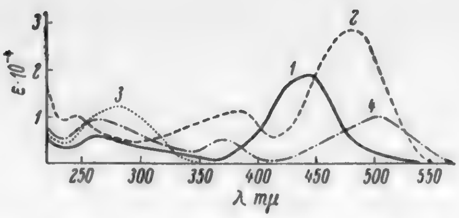


Fig. 2. Absorption spectra of monoanil (I). 1) In ethyl alcohol; 2) in ethyl alcohol + 250 equiv. NaOH; 3) in ethyl alcohol + 10 equiv. HCl; 4) in ethyl alcohol + 250 equiv. NaOH + 300 equiv. HCl.

Since the Na-enolate of the monoanil derived from aniline is unstable the equilibrium is gradually displaced toward the monoanil, which causes a heightening of the color. For complete conversion of the monoanil to the enolate a definite excess of alkali is necessary, after which further addition of alkali has no effect on the absorption; for the aniline derivative this excess is equal to 25 equiv. of NaOH. We noted above, that addition

TABLE 3

Change in Absorption Maxima of Glutaconic Aldehyde Monoanil (I) in Dependence on the Time of Standing of the Solution (values of $\epsilon \cdot 10^{-4}$ are given in parentheses)

Solvent	Ethyl alcohol		Ethyl alcohol + NaOH			Ethyl alcohol + + NaOH + excess HCl	
Time (in min)	0	20	0	0.5	20	0	0.5
$\lambda_{max.}$ (in mμ)	442 (1.9)	442 (1.9)	470 (1.9)	480 (2.4)	470 (2.3)	502 (1.3)	502 (2.0)

of acid to a solution of monoanil (I) in ethyl alcohol causes the color to vanish. If an excess of acid is quickly added to an alkaline solution of the monoanil in ethyl alcohol, the color is deepened; the intensity of the band increases if the acid is added within 20-30 minutes after alkalization of the solution (Table 3). The alkali decreases the polarity of the alcoholic solution, and the acid reacts with the Na-enolate of the monoanil, forming a deeply-colored salt which slowly dissociates under these conditions. When the alkali is gradually neutralized with acid, the solution is decolorized.

Changes in the spectra of monoanil (I), due to changes in the medium, are evident on comparison of the curves shown in Figure 2. The analogy in the character of the spectra in acid and alkaline media indicates that in both cases analogous transformations in the structure of the monoanil molecule take place.

The character of the reaction of monoanils with acid and alkali is connected with the basicity of the monoanils. Thus, for instance, the 2,4-dinitromonoanil (VII) is not sensitive to acids; its absorption spectra in ethyl alcohol and in acetic acid nearly coincide. The color of this compound is markedly deepened in the presence of alkali, and it changes on transition from solvent to solvent (Figure 3). Although the absorption maxima of the 2,4-dinitromonoanil are displaced with respect to one another, the main bands lie in the same region; therefore the change of color is due to the varying stability of the anion in solvents of different polarity.

The peculiarities in the variation of the color of glutaconic aldehyde monoanils, derived from primary aromatic amines, in different solvents apparently could be explained by the presence of "mobile" hydrogen on the amino-group nitrogen, which increases the degree of reaction of the monoanil with the solvent. This hypothesis is partly confirmed; the change in the absorption of the N-methylmonoanil (VIII) [10] on transition

from solvent to solvent is less than that for the unsubstituted monoanil (I) (Table 1), but it, also, is independent of the polarity of the solvent.

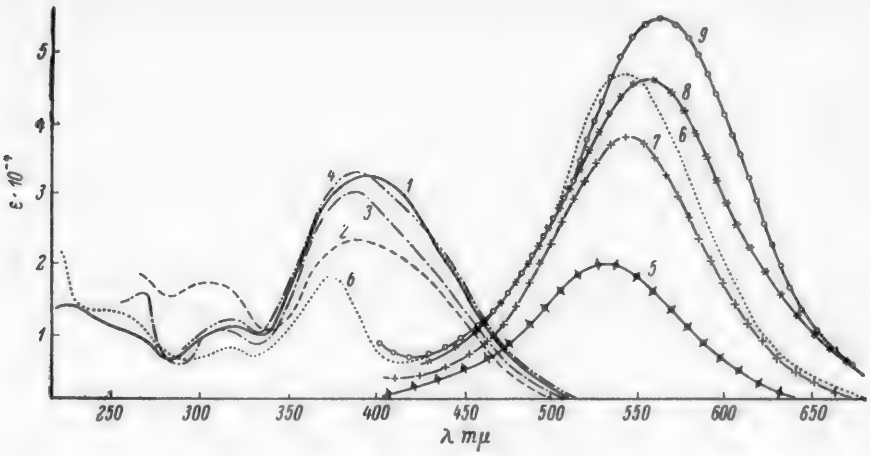


Fig. 3. Absorption spectra of monoanil (VII). 1) In ethyl alcohol; 2) in n-butyl alcohol; 3) in dichloroethane; 4) in acetic acid; 5) in methyl alcohol + NaOH; 6) in ethyl alcohol + NaOH; 7) in n-butyl alcohol + NaOH; 8) in dichloroethane + NaOH; 9) in acetone + NaOH.

Replacement of amino-group hydrogen by alkyl causes a pronounced hypsochromic shift of the absorption maximum; in benzene, for instance, the shift is equal to 118 mμ, which may be due to a decrease of conjugation in the molecule. However, a formula with an open pentamethine chain terminated by groups of diverse character cannot explain either the cause of the pronounced heightening of color or that of other peculiarities in the behavior of the N-methylmonoanil. Unlike the case of the unsubstituted monoanil (I), alkali does not affect the displacement of the absorption maximum of the N-methylmonoanil (VIII), which confirms the tautomeric conversion of monoanil (I). In the presence of hydrogen chloride the color is not deepened in any of the solvent investigated, but the monoanil is decomposed; in the spectrum the band of glutaconic aldehyde in an acid medium [11] (Figure 4) appears. All these peculiarities in the absorption of the N-methylmonoanil are easily explained if it is assumed that the latter has a cyclic structure (VIIIa) [12].

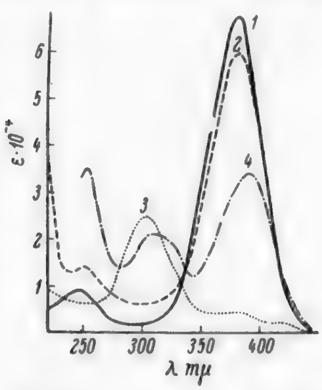
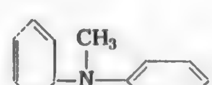


Fig. 4. Absorption spectra of monoanil (VIII). 1) In ethyl alcohol; 2) in ethyl alcohol + 250 equiv. HCl; 3) in ethyl alcohol + 250 equiv. HCl; 4) in acetic acid.



(VIIIa)

The facts, stated above, on the color change of glutaconic aldehyde monoanils confirm the hypothesis, advanced earlier, [4, 5], that the variation of color of non-saltlike dyes in different solvents depends on the structure of the complexes formed by the dye with the solvent. They, in turn, are in accord with the investigations of N. A. Izmailov [13], who established that the variation of acid dissociation constants in different solvents is due to the formation of acid-solvent complexes.

The variation in the color of monoanils in different solvents in the presence of acids and alkali is convincing evidence of the fact that there is no difference in principle between solvatochromy and halochromy. In both cases an acid-base reaction takes place. The variation of the color in different solvents is due to dis-

placement of the equilibrium: dye + solvent (acid, base) $\rightleftarrows$ complex (salt).

The absorption spectra were determined with an SF-4 spectrophotometer in the ultraviolet and with an SF-2M in the visible region. The solvents were purified by the methods usually employed for spectroscopy.

SUMMARY

1. The absorption spectra of eight glutaconic aldehyde monoanils in various solvents, alone and in the presence of acids and alkali, have been investigated.

2. It has been shown that the variation in the absorption of glutaconic aldehyde monoanils in different solvents is connected with the structure of the complexes formed by the monoanil with the solvent if a reaction between them is possible.

3. Certain views have been expressed concerning the causes of variation of the color of glutaconic aldehyde monoanils in different solvents in the presence of acids and alkali. It has been shown that there is no difference in principle between solvatochromy and halochromy.

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INVESTIGATION OF ANODE DEPOSITS FORMED IN THE ELECTROLYSIS OF SOLUTIONS OF CERTAIN THALLIUM SALTS. III

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The study of the properties of thallium and its compounds is now an important problem of chemical science. This element is finding ever-increasing practical application. Thallium is an accessory element in lead-zinc ores. In the present method of electrolytic separation of zinc at the cathode the possibility of formation of thallium oxides at the anode, in the form of anode deposits, should be taken into account; such deposition of thallium oxides on the anode may take place in the electrolytic preparation of thallium.

The possibility of obtaining anode deposits from solutions of thallium salts (nitrate and sulfate) has repeatedly been pointed out by various authors. However, neither the conditions for obtaining anode deposits nor the composition of the latter was definitely established in earlier works. It was assumed that anode deposits consists of higher oxides of thallium, but the oxidation states were not precisely specified. Some authors consider the deposits to be composed of oxides of tervalent thallium [1-7]; others consider them to consist of a mixture of the oxides of 3- and 4-valent thallium [4, 5] or a peroxide of thallium [8], similar to the peroxides of potassium, rubidium, and other metals. The addition of various organic substances such as alcohol, oxalic or benzoic acid, acetone, etc., was considered a necessary condition for carrying out electrolysis.

The purpose of the present work is to answer the following questions: 1) under what conditions of electrolysis of thallium-salt solution the anode deposits are best formed; 2) what the composition of these deposits is; i.e., whether they are oxides of thallium in one valence state or another or have a more complicated composition; 3) whether complex formation affects the composition of the deposit or the conditions of its production.

EXPERIMENTAL

For investigation of the anode deposits obtained on electrolysis of thallium-salt solutions we chose the following soluble thallous salts: the nitrate, fluoride, sulfate, and carbonate and the complex salts of silver nitrate with thallium nitrate and of ammonium nitrate with thallium nitrate, having the compositions $Ag[Tl(NO_3)_2]$ and $NH_4[Tl(NO_3)_2]$; of these, four salts were investigated for the first time.

Saturated solutions were electrolyzed in electrolyzers of 100-300 ml capacity, at relatively low current densities from 12 to 20 ma/cm^2 and an electrode potential of 2-2.5 v. Platinum plates, 1 cm^2 in area, served as electrodes.

When the stated conditions are met, finely crystalline, black deposits with a metallic luster are produced in the form of a close-fitting film on the anode, from electrolytes without organic admixtures. The highest possible concentration of solutions and low current strength are essential. Otherwise, gas bubbles begin to appear at the anode together with the deposit, and the latter is obtained in an extremely fine, brownish form and does not adhere to the electrode.

We carefully washed the electrolyte from the shiny, black deposit obtained at the anode and dried the deposit to constant weight at 110-120°. It was very stable to washing with water and drying up to 170°. Concentrated sulfuric acid did not dissolve the deposit, and on heating, evolution of oxygen, which would have occurred in the case of peroxide formation at the anode, was not observed. The deposit was readily soluble

at room temperature in concentrated and dilute hydrochloric acid without evolution of chlorine, and the precipitate described by Gallo and Cenni [9] was not formed at all.

The anode deposits were subjected to a detailed analytical determination of their content of thallium, total oxygen, and higher oxides, as well as any possible additional components.

Thallium was determined by two methods – precipitation as $Tl(OH)_3$ and precipitation as TlI. The total amount of oxygen contained in the anode deposit was determined by the method of reducing it with hydrogen and collecting the water formed. We determined the amount of oxygen in higher oxides, easily detached in the presence of any reducing agent, firstly by the usual method of reducing the oxides with oxalic acid and subsequently precipitating the excess acid as calcium oxalate monohydrate, and secondly by measuring the volume of oxygen evolved from the deposits on heating the latter at 700-750° in a current of carbon dioxide (used for removal of oxygen). The acid ions contained in the deposit were determined in each case by means of the appropriate reagents. The fluorine found in the deposit was quantitatively determined by the volumetric method through the reaction

$$AlCl_3 + 6NaF = Na_3[AlF_6] + 3NaCl.$$

The standard solutions of sodium fluoride and aluminum chloride were prepared by the method developed by I. M. Tananaev.

Average Results of Analyses of Deposits Obtained on Electrolysis of Thallium Salts

Element determined	Found (in %) in anode deposit from:						Calculated (in %) for	
	$TlNO_3$	$Ag[Tl(NO_3)_2]$	$NH_4[Tl(NO_3)_2]$	TlF	Tl_2SO_4	Tl_2CO_3	Tl_2O_3	$Tl_2O_3 \cdot HF$
Thallium								
a) determination as Tl_2O_3	89.24	89.26	89.33	85.79	87.34	89.10	89.49	85.78
b) determination as TlI	—	—	—	—	87.59	89.30	—	—
Oxygen								
a) total quantity	10.42	10.49	10.51	10.14	—	10.54	10.51	10.07
b) evolved on heating	—	—	—	—	6.99	6.57	7.00	—
c) participating in the oxidation of oxalic acid	6.98	6.89	6.90	—	7.15	6.99	7.00	—
Fluorine	—	—	—	3.94	—	—	—	3.99
Sulfate ion	—	—	—	—	1.78	—	—	—
Tl_a/Tl_c ratio	0.502	0.503	0.504	0.50	0.49	0.50	0.50	0.50

The analytical results are given in the summary table. From the data obtained it follows that anode deposits from the nitrate, the carbonate, and the complex salts consist only of thallium trioxide. The anode deposit from thallium fluoride contains fluorine. On the basis of analysis the formula $Tl_2O_3 \cdot HF$ should be assigned to it; this is in accord with cited data [10].

Analysis of the anode deposit from thallium sulfate showed the presence of sulfate ion in the amount of 1.78% on the average. The anode deposit obtained from thallous sulfate solutions apparently consists of thallium trioxide with an admixture of sulfate ion in some undetermined form.

For the purpose of a more accurate determination of the composition of the anode deposits obtained on electrolysis of thallous-salt solutions, X-ray analyses of all the anode deposits, as well as a parallel analysis of pure, chemically prepared thallic oxide, were conducted in the Laboratory of Dielectric Physics of the Physical Institute of the USSR Academy of Sciences. The purity of the orginal salts was checked by spectral

Fig. 1. X-ray diffraction pattern of chemically-prepared Tl_2O_3.

Fig. 2. X-ray diffraction pattern of anode deposit from $TlNO_3$.

Fig. 3. X-ray diffraction pattern of anode deposit from TlF.

Fig. 4. X-ray diffraction pattern of anode deposit from Tl_2SO_4.

Fig. 5. X-rya diffraction pattern of anode deposit from Tl_2CO_3.

analysis, which revealed only unweighable traces of Pb and Zn in the nitrate prepared by us from metallic thallium.

X-ray diffraction patterns of the anode deposits obtained on electrolysis of thallium nitrate and carbonate solutions and the X-ray pattern of chemically prepared thallium trioxide have identical lines, which exactly coincided when superposed.

X-ray diffraction patterns of the anode deposits from solutions of thallium fluoride and sulfate and X-ray patterns of thallic oxide chemically prepared from the salt have common lines corresponding to Tl_2O_3; besides, the X-ray patterns of these anode deposits contain many additional lines, which evidently belong to the fluoride and sulfate ions present in the deposits.

X-ray diffraction patterns of anode deposits are shown in Figures 1-5.

In order to confirm the composition of the deposits obtained on the anode we used not only analytical and X-ray methods, but also a method proposed earlier [11], which consists in determining the ratio of the quantity of thallium in the anode deposit (Tl_a) to the quantity of thallium which separated out at the cathode (Tl_c) during the same time. If a deposit containing two tervalent thallium atoms is formed on the anode as a result of the anodic oxidation of thallium from the univalent state to the tervalent, the total number of electrons lost by the thallium in oxidation at the anode is equal to four: $2Tl^+ - 4e^- \rightarrow 2Tl^{+++}$. At the cathode, then, four univalent thallium atoms may be reduced during the same time: $4Tl^+ + 4e^- \rightarrow 4Tl$. Therefore the ratio of the quantity of thallium deposited on the anode to the quantity of thallium deposited on the cathode, Tl_a/Tl_c, must be equal to 0.5. In a great number of experiments on the electrolysis of thallium salts we were able to confirm this ratio in all cases (see summary table).

SUMMARY

1. It has been shown that in the electrolysis of solutions of thallous salts – the nitrate, fluoride, sulfate, and carbonate and complex salts of the compositions $Ag[Tl(NO_3)_2]$ and $NH_4[Tl(NO_3)_2]$ – black, extremely stable, finely-crystalline deposits, which have a metallic luster and closely fit the electrode, are obtained at the platinum anode. In the literature the electrolysis of solutions of thallium nitrate and sulfate, only, is described. Solutions of the other four salts were electrolyzed for the first time.

2. It has been shown that the anode deposit is thallium trioxide, Tl_2O_3. The deposit obtained from thallium sulfate solution contains an admixture of sulfate ion in the amount of 1.78%; the anode deposit from the fluoride solution has the composition $Tl_2O_3 \cdot HF$.

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IRREVERSIBLE-COMMON SYSTEM OF SODIUM AND POTASSIUM BUTYRATES AND THIOCYANATES

N. M. Sokolov and E. I. Pochtakova

The immediate task of the present work is to investigate the direction of the exchange reaction between sodium and potassium butyrates and thiocyanates in melts containing them. The given common system is one of a series of systems composed of salts of thiocyanic acid and of fatty acids; the over-all purpose of the study of these systems is to determine the dependence of the direction of the exchange reaction on the structure of the fatty-acid salt radical [1].

Potassium thiocyanate has a polymorphic transformation at 143° [2], whereas sodium thiocyanate, to judge from literature data [2], has no polymorphic transformations. An investigation by one of us [3] revealed that polymorphism occurs in the case of butyrates. Thus, sodium butyrate has transformations at 117, 232, 252, and 316°, and potassium butyrate at 190, 280-285, and 345°.

EXPERIMENTAL

All the work was done by the visual-polythermic method, the usual procedure being employed. The temperature was measured with a nichrome-constantan thermocouple.

Commercial thiocyanate preparations were twice recrystallized, first from water and then from alcohol. Sodium and potassium butyrates were synthesized from the acid and C. P. bicarbonates according to directions published earlier [4]. The salts obtained were recrystallized from butanol. Melting points: sodium butyrates, 330°; potassium butyrate, 404°; sodium thiocyanate, 311°; potassium thiocyanate, 177°. In Table 1-3 all compositions are given in molar percentages, and the temperatures of formation of the first crystals are stated.

Binary Sub-Systems

1. The NaCNS–KCNS system. This was first described as a system with eutectic melting [2]. According to our data, the two branches of the liquidus curve intersect at 126° and 74% KCNS (Table 1, Figure 1).

2. The C_3H_7COONa–C_3H_7COOK system was investigated for the first time; it gives a continuous series of solid solutions (Table 1, Figure 1).

3. The NaCNS–C_3H_7COONa system. This was described earlier by one of us [5]. The three branches of the liquidus curve intersect at the eutectic point 262° and 51.5% C_3H_7COONa, and the transition point, 268° and 68.5% C_3H_7COONa (Table 1, Figure 1).

4. The KCNS–C_3H_7COOK system. Investigated for the first time. Here complex formation takes place. The three branches of the liquidus curve intersect at the eutectic point, 170° and 6.5% C_3H_7COOK, and the transition point, 335° and 82% C_3H_7COOK. The composition $6C_3H_7COOK \cdot KCNS$ is proposed for the addition compound (Table 1, Figure 1).

Diagonal Sections

The stable diagonal section KCNS–C_3H_7COONa. The phase diagram consists of two branches, which intersect at the eutectic point, 165° and 4% C_3H_7COONa (Table 2, Figure 2).

TABLE 1

Binary Systems

Na, K ‖ CNS		Na, K ‖ C_3H_7COO		Na ‖ CNS, C_3H_7COO		K ‖ CNS, C_3H_7COO	
KCNS (mol %)	temperature	C_3H_7COOK (mol %)	temperature	C_3H_7COONa (mol %)	temperature	C_3H_7COOK (mol %)	temperature
0	311°	0	330°	0	311°	0	177°
5	304	5	339	5	307	2.5	176
10	298	10	348	10	304	5	174
15	292	15	356	15	302	6.5	170
20	282	20	364	20	300	7.5	173
25	272	25	370	25	298	10	183
30	262	30	375	30	295	15	204
35	251	35	380	35	290	20	215
40	238	40	385	40	287	25	224
45	224	45	389	45	280	30	232
50	211	50	393	50	269	45	260
55	195	55	396	51.5	262	55	278
60	178	60	399	55	263	65	301
65	162	65	402	60	264	70	310
70	142	70	405	65	266	75	322
72.5	131	75	406	68.5	268	77.5	327
74	126	80	406	75	275	80	335
75	127	85	405	70	291	82	335
80	139	90	405	85	316	82.5	337
85	150	95	404	90	324	85	342
90	158	100	404	95	328	90	364
95	168			100	330	95	379
100	177					100	404

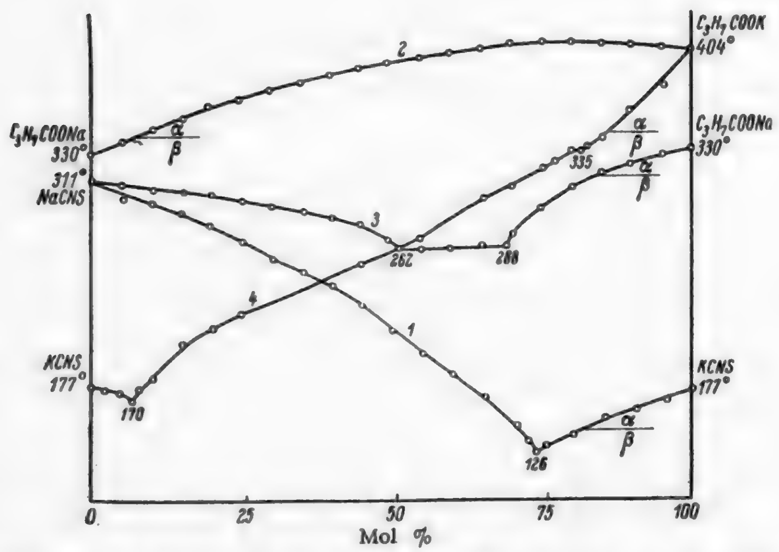

Fig. 1. Phase diagrams of binary systems. 1) NaCNS–KCNS, 2) C_3H_7COONa–C_3H_7COOK, 3) NaCNS–C_3H_7COONa, 4) KCNS–C_3H_7COOK.

The metastable diagonal section NaCNS–C_3H_7COOK. Potassium butyrate forms solid solutions with the exchange product (C_3H_7COONa). Therefore the phase diagram consists only of two branches, which intersect at 239° and 26% C_3H_7COOK (Table 2, Figure 2).

Internal Sections

In order to reveal the surface of crystallization of the system we investigated 20 internal sections, the disposition of which is given in Figure 3. Crystallization curves are shown in Figure 4.

TABLE 2

Diagonal Sections

Stable diagonal section KCNS–C_3H_7COONa		Metastable diagonal section NaCNS–C_3H_7COOK		Stable diagonal section KCNS–C_3H_7COONa		Metastable diagonal section NaCNS–C_3H_7COOK	
C_3H_7COONa (mol %)	temperature	C_3H_7COOK (mol %)	temperature	C_3H_7COONa (mol %)	temperature	C_3H_7COOK (mol %)	temperature
0	177°	0	311°	45	263°	50	267°
2.5	169	5	302	50	265	55	272
4	165	10	292	60	273	60	278
5	176	15	280	65	278	65	285
10	217	20	260	70	285	70	297
15	237	25	242	75	295	75	317
20	248	26	239	80	307	80	336
25	254	30	247	85	318	85	348
30	259	35	252	90	326	90	364
35	262	40	257	100	330	95	387
40	264	45	265			100	404

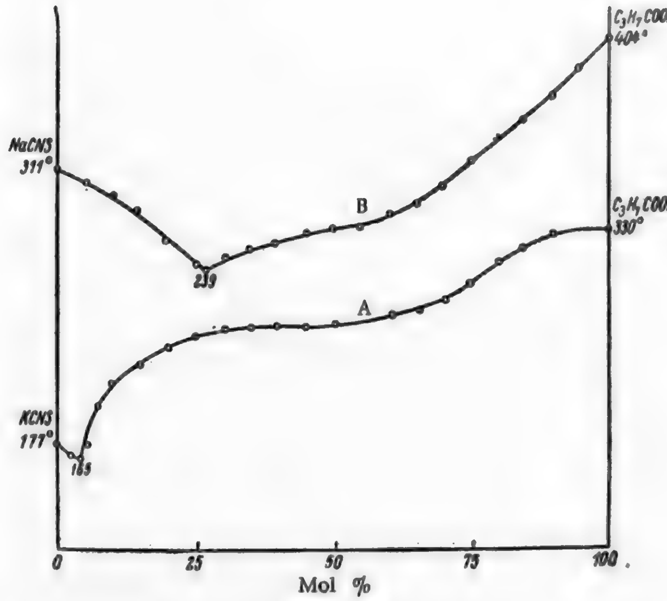

Fig. 2. Diagonal sections of the system. A) Stable diagonal section; B) metastable diagonal section.

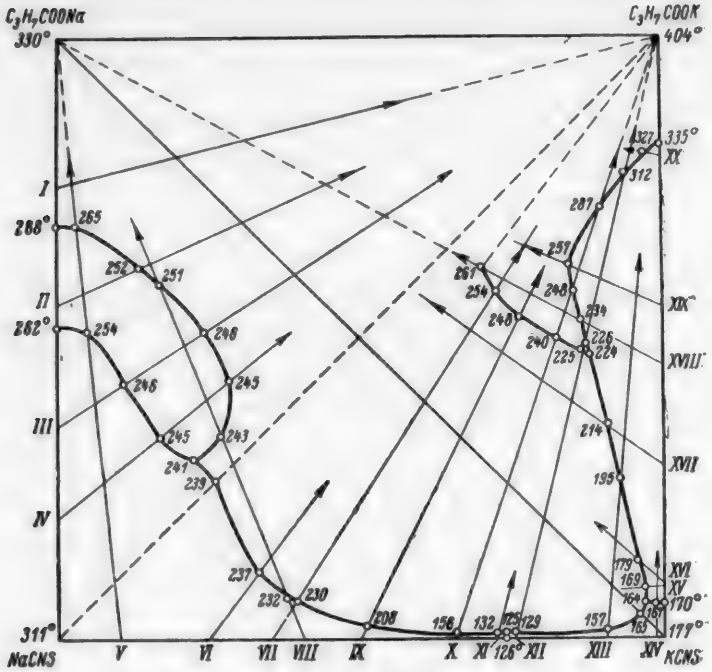

Fig. 3. Direction of internal sections.

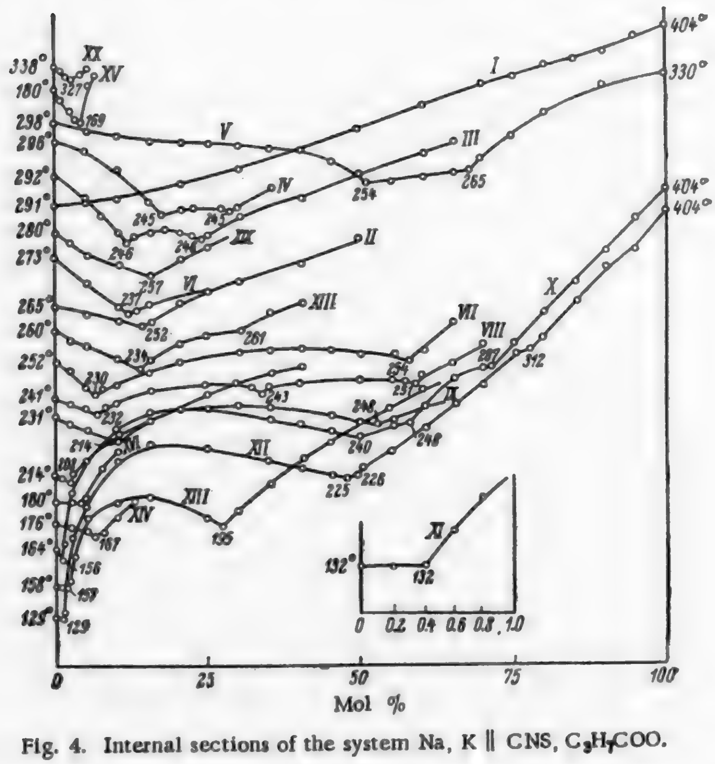

Fig. 4. Internal sections of the system Na, K ‖ CNS, C_3H_7COO.

DISCUSSION

As a result of the investigation of binary sub-systems of the common system, diagonals, and 20 internal sections, the projection of the three-dimensional diagram was plotted on the square of composition. The system investigated is a diagonal, irreversible-common system, the equilibrium in which is shifted toward the stable salt pair C_3H_7COONa and KCNS, which are not the most refractory components of the present system. Owing to the lack of data on heats of formation both for butyrates and for their addition compounds, it is possible to judge whether the direction of the reaction corresponds to the conventional heat of reaction.

The surface of the liquidus of the system consists of the following fields; The field of solid solutions of the butyrates – 73.7% of the total surface (below 260° it breaks up into potassium butyrate and sodium butyrate fields); that of NaCNS – 13.2%; that of KCNS – 0.5%; that of the addition compound $6C_3H_7COOK \cdot KCNS$ – 6.7%; that of the addition compound $4C_3H_7COONa \cdot NaCNS$ – 5.9% (Figure 5).

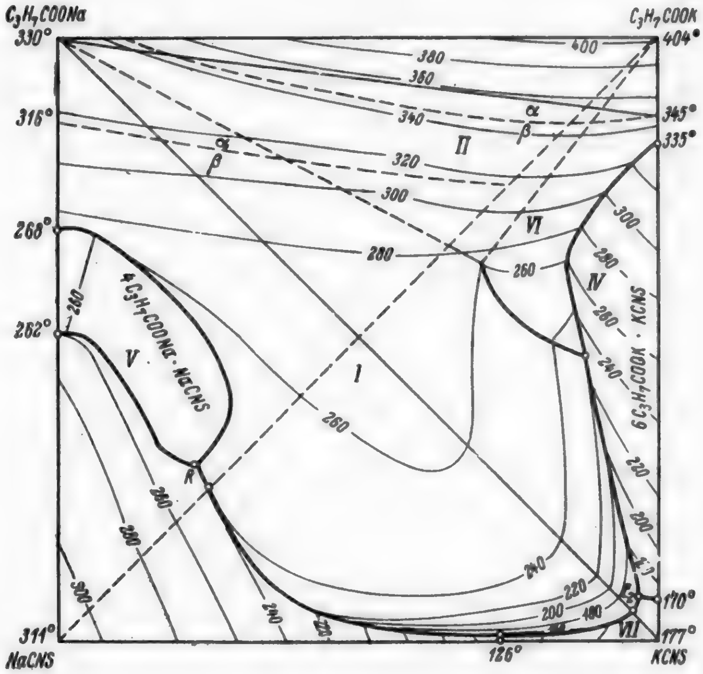

Fig. 5. Projection of the three-dimensional diagram of the system on the square of composition.

The stable diagonal section C_3H_7COONa–KCNS and the section passing from the hypothetical pole of the addition compound $6C_3H_7COOK \cdot KCNS$ to the C_3H_7COONa vertex divide the entire surface of the square of the common system into three phase triangles: 1) C_3H_7COONa–NaCNS with the triple eutectic point E_1 and the transition point R; 2) KCNS–$6C_3H_7COOK \cdot KCNS$–C_3H_7COONa with the triple eutectic point E_2; 3) $6C_3H_7COOK \cdot KCNS$–C_3H_7COONa–C_3H_7COOK with the triple transition point P. In order to determine the temperature and composition of the triple invariant points more precisely, a projection of the cocrystallization lines was plotted on the NaCNS–KCNS side (Figure 6); the temperatures and compositions corresponding to the invariant points are given in Table 3.

Comparison of the results of investigation of the present system with systems investigated earlier – Na, K ‖ HCOO, CNS; Na,K ‖ CH_3COO, CNS and Na, K ‖ C_2H_5COO, CNS [1] – shows that in all these systems the equilibrium is irreversibly shifted toward the formation of potassium thiocyanate and the sodium salt of the fatty acid. Of the salts of the stable pair in these systems the most stable is the sodium salt of the fatty acid, which, as the number of carbon atoms in the salt molecule increases, drives the KCNS further back along the stable diagonal. Thus, in the system formed by formates the fraction of KCNS on the stable diagonal amounts

TABLE 3

Triple Invariant Points

Designation of points	Temperature	Composition at the invariant point
E_1	125°	73.6% KCNS, 0.4% C_3H_7COONa, 26% NaCNS
R	241	23% KCNS, 30% C_3H_7COONa, 47% NaCNS
E_2	164	93.5% KCNS, 2.5% C_3H_7COONa, 4% C_3H_7COOK
P	234	52.5% KCNS, 12.5% C_3H_7COONa, 35% C_3H_7COOK

to 28.5%; in the acetate system it is 14.5%; in the propinate, 7.5%; in the butyrate, 4%. If A. P. Palkin [6] is followed further and the stable triangles in each of these systems, i.e., triangles of the type: sodium salt of

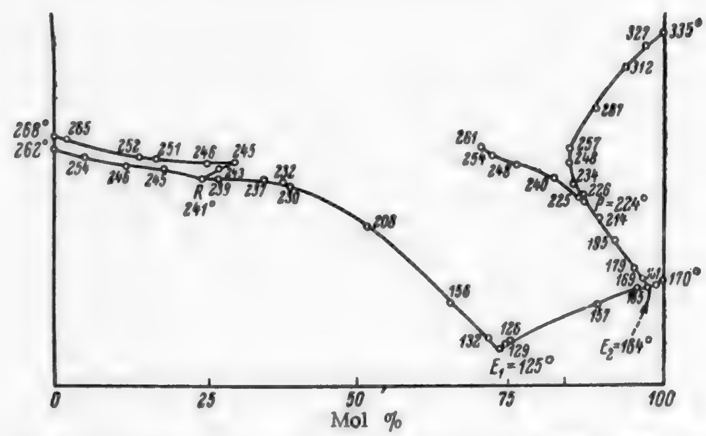

Fig. 6. Projection of cocrystallization lines on the NaCNS–KCNS side.

the fatty acid–sodium thiocyanate–potassium thiocyanate, are considered separately, then, as is evident from Table 4, the area falling to the share of the sodium salt of the fatty acid steadily increases as the number of carbon atoms per molecule of the latter increases. All this indicates that as the number of carbon atoms in the salt molecule increases, the degree of irreversibility in the system grows.

TABLE 4

Relative Sizes of Fields

System	Size of field (in % of the total surface of the field of the stable triangle)	
	field of KCNS	field of sodium salt of fatty acid
Na, K ‖ HCOO, CNS	12.3	40.9
Na, K ‖ CH_3COO, CNS	4.2	65.6
Na, K ‖ C_2H_5COO, CNS	2.2	73
Na, K ‖ C_3H_7COO, CNS	1.2	61 *

In conclusion, we regard it as a pleasant duty to thank A. G. Bergman for valuable advice.

*Part of the C_3H_7COONa is used up in the formation of the addition compound $4C_3H_7COONa \cdot NaCNS$.

SUMMARY

1. The irreversible-common system of sodium and potassium butyrates and thiocyanates has been investigated.

2. The liquidus curves of the binary systems $C_3H_7COONa-C_3H_7COOK$ and $KCNS-C_3H_7COOK$.

3. As the number of carbon atoms in the salt radical increases, the degree of irreversibility in systems formed by salts of a fatty acid and sodium and potassium thiocyanates grows.

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TOWARD THE QUESTION OF CONTACT FUSION OF CRYSTALS

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In a work by M. Kh. Gluzman and V. P. Rubtsova [1], devoted to contact fusion of three- and four-component organic systems giving eutectics, there are a number of errors which mislead the reader with regard to the present state of the problem.

The authors hold that contact fusion in ternary and quaternary eutectic systems may be observed on contact of a specimen of a binary (ternary) eutectic with a piece of a substance giving a ternary (quaternary) eutectic with the specimen. However, another method of detecting contact fusion of ternary (quaternary) eutectic systems has also been described [2]. Contact fusion occurs also on heating a mixture of powders of the three (four) components. In this case increase in the dispersity of the components lead to increase in the total contact surface among them, thereby facilitating contact fusion.

The authors write that contact fusion of ternary and quaternary eutectic systems was described by S. V. Avakian and N. F. Lashko [3] in 1949 and do not mention that it had already been described by D. D. Saratovkin and P. A. Savintsev [4] in 1947. Contact fusion of organic substances had been described even earlier [5].

The phenomenon of contact fusion may be explained [2] by the difference between interactions of homogeneous and heterogeneous atoms; in the solid state, interaction between homogeneous atoms predominates, whereas that between heterogeneous atoms predominates in the liquid state. The temperature of contact fusion is that temperature at which the transition from one type of particle interaction to the other takes place.

Temperature of Contact Fusion of Substances Forming Solid Solutions

Component		Melting point		Temperature of contact fusion
A	B	t_A	t_B	
NaCl	KCl	800°	790°	660°
KBr	NaBr	768	770	670
KCl	KBr	790	768	750
NaI	KI	700	710	580
KCl	NaBr	790	770	646
NaBr	NaI	770	700	640
NaBr	KI	770	710	560

It might be supposed that we encounter a similar phenomenon not only in eutectic systems, but also in systems forming solid solutions. Therefore the phenomenon of contact fusion may be expected in this case as well. To confirm the above we performed experiments with the crystals listed in the table.

Crystals A and B were brought into contact and heated. As the temperature $\underline{t}°$ was reached, liquid appeared at the point of contact. Our X-ray investigations of the solidified melts obtained in contact fusion have confirmed that we are dealing with solid solutions. The melt of the KCl-NaCl system is an exception. In this case the roentgenograms indicate a mixture of components. Thermal analysis of the KCl–NaCl system indicates solid solutions which separated into two phases at temperatures below 495°. Evidently this also explains the form of the KCl–NaCl system roentgenogram.

Substances forming solid solutions can diffuse into each other, which leads to their sintering at a temperature lower than the melting points of the components. In order to ascertain the effect of diffusion on contact fusion we held the specimens in contact at a temperature 50° below that of contact fusion for 10-20 hours; after this treatment we observed no sintering of the specimens. Evidently diffusion processes have no effect on the phenomenon of contact fusion of crystals.

The experiments which were performed provide grounds for the assertion that contact fusion occurs both in the case of substances forming eutectics and in that of substances forming solid solutions. The easy fusibility of the eutectics and solid solutions cannot be explained by the structural properties of the eutectic or solid solution. Therefore the temperature of contact fusion is a physical quantity determined by the disposition of adjacent particles with respect to one another.

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INVESTIGATION OF THE REACTION OF PHENYL-β-NAPHTHYLAMINE WITH ORGANIC ACIDS BY THE METHODS OF PHYSICO-CHEMICAL ANALYSIS

N. K. Tsvetkova and D. E. Dionis'ev

The introduction of a benzene nucleus into an aromatic-amine molecule markedly lowers its activity with respect to organic acids. It was of interest to ascertain how the replacement of one benzene nucleus in a secondary-amine molecule by a naphthalene nucleus affects its ability to react with organic acids.

The reaction of phenyl-β-naphthylamine with organic acids has not been studied before by anyone.

EXPERIMENTAL

Phenyl-β-naphthylamine was recrystallized several times from ethyl alcohol and dried in a desiccator in a current of warm air; m.p. 106.3°. Trichloroacetic acid of C. P. grade was distilled three times and kept in sealed ampules; m.p. 59°, b. p. 197°. Salicylic acid of C. P. grade was purified by repeated recrystallization and had m. p. 159.8°. Succinic acid of C. P. grade had m. p. 184.5° after recrystallization. Adipic acid of C. P. grade had m. p. 151°.

Measurements of viscosity, density, and electrical conductivity were performed in a glycerol thermostat which permitted maintenance of the temperature within a ±0.1° range. The mixtures were prepared by the method of separate weighed portions. Concentrations were calculated in molar percentages; viscosities were expressed in centipoises.

1. The phenyl-β-naphthylamine–trichloroacetic acid system was studied by us with regard to melting point, viscosity, density, and specific electrical conductivity (Figure 1).

The liquidus curve has a maximum corresponding to 50 mol. % phenyl-β-naphthylamine, which indicates the formation in the solid phase of a compound with equimolar composition, $\beta\text{-}C_{10}H_7NHC_6H_5 \cdot CCl_3COOH$, having m.p. 94.5°. Eutectic points; 88.5° and 60 mol. % phenyl-β-naphthylamine, and 33° and 12 mol. % of the latter.

The viscosity and density of this system were studied at 90, 100, and 110°. At 90 and 100° these properties, as well as the electrical conductivity, could not be investigated completely, since mixtures with a high-phenyl-β-naphthylamine content were not supercooled at the stated temperatures. The density curves were convex to the concentration axis, which indicates the absence of shrinkage in the system. The viscosity curve at 90° has a maximum corresponding to 40 mol. % phenyl-β-naphthylamine in the mixture. As the temperature rises, the maximum is displaced toward higher concentrations of trichloroacetic acid, i. e., the less viscous component. On the curves of the absolute temperature coefficient the maximum is retained. Thus the form of the viscosity curves indicates that the components are combined in the liquid phase. The shift of the maximum on the viscosity curves toward the less viscous component indicates, in the opinion of V. V. Udovenko [1], that the components form a new compound in the liquid phase. It is difficult to judge the composition of the compound from the position of the maximum in the given case.

The electrical conductivity of the mixtures at first increases slowly, but then, beginning at 40 mol. % phenyl-β-naphthylamine, rises sharply, passes through a maximum corresponding to 10 mol.% phenyl-β-naph-

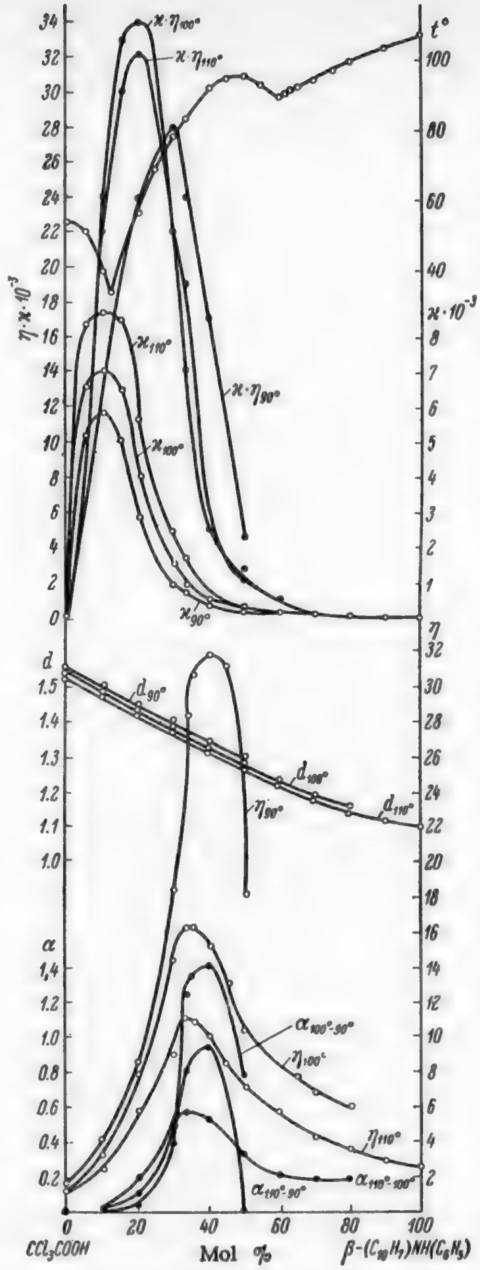

Fig. 1. Phenyl-β-naphthylamine–trichloroacetic acid system. Liquidus (t), viscosity, (η), density (d), and specific (χ) and corrected (η, χ) electrical conductivity curves.

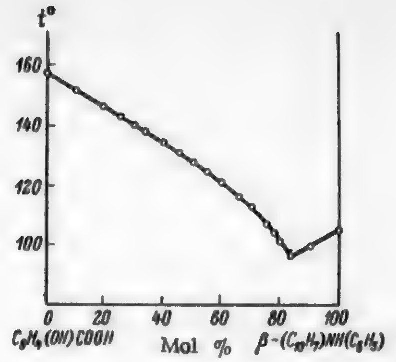

Fig. 2. Liquidus curve of the phenyl-β-naphthylamine–salicylic acid system.

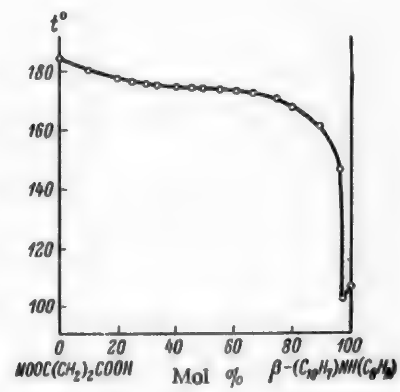

Fig. 3. Liquidus curve of the phenyl-β-naphthylamine–succinic acid system.

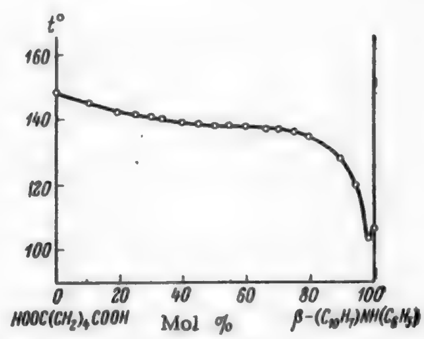

Fig. 4. Liquidus curve of the phenyl-β-naphthylamine–adipic acid system.

thylamine, and falls sharply to the value for pure trichloroacetic acid. On correcting the electrical conductivity for viscosity the maximum is only slightly displaced. According to M. I. Usanovich [2] curves having this form indicate an acid-base reaction in the system, although the position of the maximum does not correspond to the composition of the compound.

2. The phenyl-β-naphthylamine–salicylic acid system was investigated by us with regard only to melting points (Figure 2). The two branches of the curve intersect at the eutectic point, 98° and 85 mol. % phenyl-β-naphthylamine. The form of the liquidus curve indicates that no chemical reaction between the components occurs in the solid phase.

3. The phenyl-β-naphthylamine–succinic acid system was investigated with regard to melting points (Figure 3). The succinic acid branch is a curve, slightly inclined to the composition axis, which falls abruptly at 80 mol.% phenyl-β-naphthylamine; the phenyl-β-naphthylamine branch is merely a small fragment. Both branches intersect at the eutectic point, 103° and 98 mol. % phenyl-β-naphthylamine. The type of liquidus curve is characteristic of systems in which partial mutual miscibility of the components is approached.

4. The phenyl-β-naphthylamine–adipic acid system (Figure 4). The liquidus curve is extremely similar to that of the preceding system. The adipic acid branch is a sloping, slightly bent curve which falls abruptly from 80 mol. % to the eutectic point (104° and 99 mol. % phenyl-β-naphthylamine). Here, also, we have an approach to partial mutual miscibility of the components.

The investigation revealed that phenyl-β-naphthylamine reacts with trichloroacetic acid like diphenylamine. In the other systems studied there is no chemical reaction between the components. Thus, introduction of a naphthalene nucleus in the place of a benzene ring in a molecule of a secondary aromatic amine has almost no effect on the character of the reaction with organic acids, and the capacity of phenyl-β-naphthylamine for complex formation is still greatly diminished.

SUMMARY

1. The systems formed by phenyl-β-naphthylamine with salicylic, succinic, and adipic acids have been studied with regard to melting points. Phase diagrams have been obtained for the stated systems, which indicate that there is no chemical reaction between the components.

2. The sytem formed by phenyl-β-naphthylamine with trichloroacetic acid has been studied with regard to melting points, viscosity, density, and electrical conductivity. On phase diagrams of the system an indication that the components react in both the solid and liquid phases has been obtained.

3. It has been established that replacement of one benzene ring in a molecule of a secondary aromatic amine by a naphthalene nucleus is not reflected in the character of the reaction of the amine with organic acids.

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COMPOUNDS OF CADMIUM AND MERCURY HALIDES WITH NICOTINE

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It was shown earlier by us [1-3] that halides of mercury, zinc, and cadmium form the following types of addition compounds with nicotine: $MeX_2 \cdot C_{10}H_{14}N_2$, $MeX_2 \cdot 2C_{10}H_{14}N_2$, $HMeX_3 \cdot C_{10}H_{14}N_2$, and $H_2MeX_4 \cdot C_{10}H_{14}N_2$, depending on the conditions of reaction. According to their composition and properties, the last two types of compounds apparently are salts of nicotine and the corresponding complex halide acids of mercury, zinc, and cadmium, some of which are known in the free state [4].

The present report is a continuation of investigations of complex compounds of mercury and cadmium halides of the last three types, which are not described in the literature. Compounds of mercuric chloride and bromide with nicotine, having the composition $MeX_2 \cdot 2C_{10}H_{14}N_2$, are readily formed on mixing stoichiometric quantities of the component substances in acetone solution.

Compounds with cadmium bromide and iodide, having the same composition, are formed like the mercury compounds, but they can be prepared also by solution of the salts in pure, hot nicotine; however, cadmium chloride reacts with nicotine only when the latter is heated.

The compounds were prepared with a slight excess of nicotine and with energetic stirring of the reaction mixture; they were washed several times with ether in a Schott filter, dried in a desiccator, and analyzed.

The compound $CdBr_2 \cdot C_{10}H_{14}H_2 \cdot HBr$ was formed by mixing aqueous solutions of equimolar quantities of its components. The precipitated crystals were dissolved in the mother liquor on heating, and the solution was concentrated with carbolene (karbolen)and filtered. The filtrate was drawn off by suction, and the crystals were washed in the filter and dried in a desiccator. In preparing the compound $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$ the starting materials consisted of equimolar quantities of cadmium oxide and nicotine and 3 mol. of hydriodic acid.

The compound $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ was readily formed when equimolar quantities of aqueous solutions of cadmium bromide and nicotine were vigorously mixed in a strongly acidic hydrobromic acid medium. The compound $CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ was prepared from equimolar quantities of cadmium oxide dissolved in excess hydriodic acid in nicotine [sic]. In both cases the crystals were filtered out from the mother liquor, washed with a little water, and dried in air and then in a desiccator.

Nicotine, acetone, $CdBr_2$, and HgI_2 of C. P. grade were used; $HgCl_2$ and $HgBr_2$ were prepared from HgO by treatment with acids, followed by sublimation. $CdCl_2$ was prepared from CdO by treatment with acid, followed by recrystallization and then dehydration at 120°.

Cadmium and mercury were determined gravimetrically as $CdSO_4$ and HgS. Halogens and nicotine were determined in the same way as before [3].

$HgCl_2 \cdot 2C_{10}H_{14}N_2$ – fine, white crystals. M. p. 107-110° (dec.). Yield 85%.

Found %: $C_{10}H_{14}N_2$ 55.22, 53.90, 53.80; Cl 12.80, 11.68, 11.60; Hg 34.00, 33.68. $HgCl_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 54.43; Cl 11.90; Hg 33.67.

$HgBr_2 \cdot 2C_{10}H_{14}N_2$ – fine, white crystals. M. p. 114-117° (dec.). Yield 83%.

Found %: $C_{10}H_{14}N_2$ 44.75, 44.45, 44.42; Br 23.52, 23.66, 23.48; Hg 31.91. $HgBr_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 44.78; Br 23.33; Hg 31.89.

$HgI_2 \cdot 2C_{10}H_{14}N_2$ was prepared from $HgI_2 \cdot C_{10}H_{14}N_2$ [5] by dissolving the latter in hot nicotine. When this solution was cooled, fine, brown crystals separated out, which after filtration, washing with acetone to remove nicotine, and drying gave a white powder with m.p. 127-128° (dec.). Yield 62%.

Found %: $C_{10}H_{14}N_2$ 42.24, 41.86; I 32.55, 33.26, 32.75; Hg 25.61, 25.04. $HgI_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 41.62; I 32.60; Hg 25.78.

$CdCl_2 \cdot 2C_{10}H_{14}N_2$ – a white, crystalline substance which began to decompose at 90° and melted at 125° with decomposition. Yield about 92%.

Found %: $C_{10}H_{14}N_2$ 63.64, 63.85, 63.60; Cl 13.44, 13.51; Cd 22.00, 22.23. $CdCl_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 63.88; Cl 13.97; Cd 22.14.

$CdBr_2 \cdot 2C_{10}H_{14}N_2$ a white, crystalline substance with m.p. 135-136°. (dec.). Yield 86%.

Found %: $C_{10}H_{14}N_2$ 54.45, 54.56; Br 26.63, 26.45; Cd 18.97, 19.11, 18.99. $CdBr_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 54.36; Br 26.79; Cd 18.84.

$CdI_2 \cdot 2C_{10}H_{14}N_2$ –a white, crystalline substance which melted at 130° (dec.). Yield 91%.

Found %: $C_{10}H_{14}N_2$ 47.02, 46.94; I 36.10, 36.73; Cd 16.08, 15.95, 16.22. $CdI_2 \cdot 2C_{10}H_{14}N_2$. Calculated %: $C_{10}H_{14}N_2$ 46.97; I 36.76; Cd 16.28.]

$CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$ –white crystals, m.p. 169-171° (dec.).

Found %: $C_{10}H_{14}N_2$ 31.56, 31.52; Br 46.59, 46.65; Cd 21.87, 21.75. $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$. Calculated %: $C_{10}H_{14}N_2$ 31.46; Br 46.52; Cd 21.80.

$CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$ – white, slightly yellowish crystals. M. p. 203-205° (dec.). Yield about 100%.

Found %: $C_{10}H_{14}N_2$ 24.15, 24.48; I 58.21, 58.18; Cd 17.05, 17.27. $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$. Calculated %: $C_{10}H_{14}N_2$ 24.70; I 58.01; Cd 17.13.

$CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ – white crystals. M. p. 205-208° (dec.). Yield 71%.

Found %: $C_{10}H_{14}N_2$ 27.49, 27.83, 27.54; Br 53.58, 53.72; Cd 18.59, 18.33, 18.71. $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$. Calculated %: $C_{10}H_{14}N_2$ 27.19; Br 53.61; Cd 18.86.

$CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ – slightly yellowish crystals. M. p. 209-210° (dec.). Yield 38%.

Found %: $C_{10}H_{14}N_2$ 20.38, 20.74, 20.26; I 64.40, 63.53; Cd 14.18, 14.12, 14.38. $CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$. Calculated %: $C_{10}H_{14}N_2$ 20.67; I 64.74; Cd 14.33.

We determined the solubilities, molar electrical conductivities, and pH values in water at 25° of the compounds of cadmium halides with nicotine, and also the previously described [1, 3] compounds of mercury and zinc halides with nicotine, having the composition $H_2MeX_4 \cdot C_{10}H_{14}N_2$, which are listed in the table.

As is evident from the data of the table, the compound $ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ has a pH of 6.31. Other zinc and cadmium compounds of the same type have pH values between 3 and 4. This is apparently due to the fact that the complex compound $ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$ is more stable and it decomposes in aqueous solution to a lesser degree than other zinc and cadmium compounds of this type.

The molecular weights of the compounds $ZnCl_2 \cdot 2C_{10}H_{14}N_2$ and $ZnBr_2 \cdot 2C_{10}H_{14}N_2$ in acetone were also ebullioscopically determined.

Found : M 446. $ZnCl_2 \cdot 2C_{10}H_{14}N_2$. Calculated: M 460.55. Found: M 573, $ZnBr_2 \cdot 2C_{10}H_{14}N_2$. Calculated: M 549.38.

It must be assumed that these substances are addition products.

The melting points of compounds containing two molecules of acid are higher than those of compounds containing one molecule of acid, and compounds of both types have higher melting points than compounds of the type $MeX_2 \cdot 2C_{10}H_{14}N_2$, obtained from organic solvents. The melting points of compounds of zinc with nicotine are higher than those of the corresponding compounds of cadmium and mercury with nicotine. Compounds containing bromine are higher-melting than chlorine compounds, whereas iodine compounds are higher-

melting than the corresponding bromine compounds in some cases, but lower-melting in others.

The solubility of compounds of the type $MeX_2 \cdot C_{10}H_{14}N_2 \cdot 2HX$ in water at 25° decreases as the atomic numbers of the metal and halogen decrease.

Compound	Solubility (in %)	Dilution (1 mole/ 1000 liters)	
		electrical conductivity	pH
$ZnCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$	50.66	620	3.24
$ZnBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$	30.10	613	3.26
$ZnI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$	5.70	450	6.31
$CdCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$	46.44	604	3.29
$CdBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$	9.30	581	3.28
$CdI_2 \cdot C_{10}H_{14}N_2 \cdot 2HI$	0.87	581	3.80
$HgCl_2 \cdot C_{10}H_{14}N_2 \cdot 2HCl \cdot H_2O$	—	450	—
$HgBr_2 \cdot C_{10}H_{14}N_2 \cdot 2HBr$	—	450	—

The molar electrical conductivity and pH indicate that in solution these compounds are completely decomposed to the original components with subsequent dissociation and hydrolysis.

SUMMARY

1. The prepared complex compounds of nicotine with cadmium bromide and iodide and the corresponding hydrohalic acids, of the type $MeX_2 \cdot C_{10}H_{14}N_2 \cdot 2HX$, are salts of nicotine and complex halide acids of cadmium, completely dissociated in aqueous solutions. It has been established that the solubility in water of compounds of this type decreases as the atomic number of the element increases.

2. Complex compounds of mercury and cadmium halides with nicotine, of the type $MeX_2 \cdot 2C_{10}H_{14}N_2$, have been prepared.

3. Tne complex compounds $CdBr_2 \cdot C_{10}H_{14}N_2 \cdot HBr$ and $CdI_2 \cdot C_{10}H_{14}N_2 \cdot HI$, have been prepared.

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LETTERS TO THE EDITOR

STUDY OF THE WALLACH REARRANGEMENT AND RELATED REACTIONS*

M. M. Shemiakin, V.I. Maimind and B. K. Vaichunaite

The mechanism of the azoxy combination reaction was recently elucidated by us [1] by means of N^{15}, and it was established that this process goes through a stage of formation of intermediate dioxy compounds. At present we have used N^{15} for the study of various isomerizations of azoxy compounds – the Wallach rearrangement and related reactions.

For this purpose $C_6H_5N^{15}H_2$ and $o\text{-}O_2N^{14}C_6H_4CHO$, synthesized from $C_6H_5N^{14}(O)=N^{15}C_6H_5$ (cf. [2, 3]), was rearranged to o- and p-hydroxyazobenzenes under varying conditions. The isotopic composition of the nitrogens in the azoxybenzene was determined by bromination followed by reductive cleavage [1], whereas that in the hydroxyazobenzenes was determined by reduction with tin in concentrated hydrochloric acid at 85-90°, aniline and aminophenols being isolated in the form of the acetyl derivatives.

It was found that in the presence of chlorosulfonic acid (-8°, 1 hour; see [4] for conditions of isolation) the rearrangement of azoxybenzene to p-hydroxyazobenzene is accompanied by complete equalization of the isotopic composition of both nitrogens.

On treatment of azoxybenzene with 83% sulfuric acid without heating (22-24°, 8.5 days) the same results were obtained; at the same time it was shown that the observed equalization of activity takes place in the rearrangement process itself and not before it, since the isotopic composition of the unreacted azoxybenzene remained practically unchanged. These results cannot be explained by the hypotheses on the mechanism of rearrangements of this kind, advanced earlier in the literature [4]. Under the described conditions, apparently, the initial stage of the process is the isomerization of the original azoxybenzene to the symmetrical oxide.

$$\mathrm{C_6H_5N^{14}(O)=N^{15}C_6H_5 \rightarrow C_6H_5N^{14}\underset{\diagdown O \diagup}{\text{——}}N^{15}C_6H_5 \rightarrow}$$
$$\mathrm{\rightarrow [{}^1/_2C_6H_5N^{14}{=}N^{15}C_6H_4OH\text{-}p + {}^1/_2C_6H_5N^{15}{=}N^{14}C_6H_4OH\text{-}p]}$$

On heating azoxybenzene with 83% sulfuric acid (90°, 8 minutes) only partial (85%) equalization of activity occurred, a higher N^{15} concentration being found at that N atom in p-hydroxyazobenzene, which was attached to the hydroxyl-bearing benzene ring; at the same time the unreacted azoxybenzene was recovered unchanged. Therefore under these conditions the conversion of azoxybenzene to p-hydroxyazobenzene exceeds by two different routes; in one of them (the main route; the scheme is given above) the rearrangement goes through a stage of oxide formation, whereas in the other (the secondary route; the scheme is given below) this stage is bypassed.

$$\mathrm{C_6H_5N^{14}(O){=}N^{15}C_6H_5 \rightarrow C_6H_5N^{14}{=}N^{15}C_6H_4OH\text{-}p}$$

* Presented at the General Assembly of the Division of Chemical Sciences of the USSR Academy of Sciences, Moscow, December 19, 1957.

In a rearrangement carried out under the influence of ultraviolet light (65 hours at 30-45° in 85% alcohol) [5] there was almost no equalization of the isotopic composition of the nitrogens in the o-hydroxyazobenzene, a higher N^{15} concentration being found at the nitrogen atom attached to the hydroxyl-bearing benzene ring. In this case the isomerization process bypasses the stage of oxide formation.

$$C_6H_5N^{14}(O)=N^{15}C_6H_5 \rightarrow C_6H_5N^{14}=N^{15}C_6H_4OH\text{-}o$$

At the same time a considerable (about 15%) degree of equalization of the isotopic composition of the nitrogens in the unreacted azoxybenzene was found. Under the influence of ultraviolet light, apparently, azoxybenzene can be reversibly isomerized very slowly from one form to the other through the intermediately formed oxide:

$$C_6H_5N^{14}(O)=N^{15}C_6H_5 \rightleftarrows C_6H_5\underset{\diagdown O \diagup}{N^{14}-N^{15}}C_6H_5 \rightleftarrows C_6H_5N^{14}=N^{15}(O)C_6H_5$$

On heating with acetic anhydride (4 hours, 230-240°) the rearrangement of azoxybenzene to o-hydroxyazobenzene takes place in the same way as under the influence of ultraviolet light, but in this case no change at all is observed in the isotopic composition of the nitrogens in the unreacted azoxybenzene.

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SYNTHESIS OF L-ACETYLALANINE FROM D,L-ALANINE

V. B. Spirichev and L. A. Shchukina

As is known, one of the most successful preparative methods for the separation of racemic amino acids into antipodes is the method proposed by Greenstein and co-workers [1, 2]. This method is based on the ability of acylase to deacylate only the L-forms of various N-acylated α-amino acids, leaving the D-forms of the acylamino acids practically unaffected.

It was shown by us that the process of deacylation of amino acids by acylase is reversible and, under certain conditions, L-acylamino acids can be synthesized from L- or D,L-amino acids by means of it. Thus, on treatment with the acylase, obtained from pig kidneys [2, 3], for 24 hours in the presence of 2 moles of sodium acetate (pH 7.8, 37°) D,L-alanine is converted to L-acetylalanine with a yield of about 15%.

The acylating ability of acylase, which we discovered, can be made the basis of a method for synthesizing L-acylamino acids directly from racemic amino acids.

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.—Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. — Publisher.